SQUIBB®


# PRODUCT REFERENCE

BOOK FOR THE MEDICAL PROFESSION

**SARABHAI CHEMICALS Ltd.**

*For the use only of registered medical practitioners or a hospital or a laboratory.*

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1975

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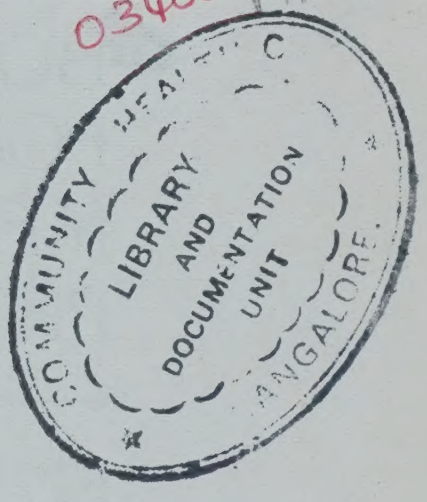


Published by N. Hukku for Sarabhai Chemicals Ltd., Shahibag House, 13, Walchand Hirachand Marg, Ballard Estate, Bombay 400 038 and printed by D. D. Karkaria at The Book Centre (Pvt.) Ltd., 103, Road No. 6, Sion (East), Bombay 400 022.

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# SQUIBB PRODUCTS

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## AMBISTRYN-S®

**Sterile Powder**

Squibb Streptomycin Sulphate

Squibb Streptomycin Sulphate is a sterile powder, readily soluble in pyrogen-free water or sterile isotonic sodium chloride solution. It is supplied in vials containing the equivalent of 0.75 Gm. and 1 Gm. pure streptomycin base.

*Indications and Dosage:*

### TUBERCULOSIS

For tuberculosis, streptomycin should be used with isoniazid and/or para-aminosalicylic acid (PAS). With a daily dose of 3 to 5 mg. isoniazid/Kg. and/or 12 to 16 Gm. PAS, intramuscular streptomycin is given either: *Daily.* 1 to 3 Gm. for adults with severe constitutional reactions and particularly with extensive pneumonia, miliary or meningeal tuberculosis. (In the latter cases the suggested daily dose of isoniazid is 7 mg./Kg. for seven days, then 3-5 mg./Kg.)

*Intermittently:* 0.75 to 1 Gm. twice weekly or every three days for adults without severe constitutional reactions or following adequate response to daily administration. For children, the average daily dose of streptomycin is 20 mg./Kg. given in divided amounts at 8 to 12 hour intervals.

| *Type of Tuberculosis* | *Treatment Duration* |
|---|---|
| pulmonary | up to 1 yr. or more depending on clinical judgment and bacterial sensitivity tests |
| surgical pulmonary (streptomycin should not be used routinely in all thoracoplasty cases) | preoperatively—depends on patient's response; postoperatively—depends on risk of tuberculous complications 4-8 wk. for surgery in presence of stable pulmonary lesions |
| mucosal (bronchial, tracheal, laryngeal, gastrointestinal, otitic) | largely a matter of clinical judgment—palliative courses generally shorter than definitive |
| serosal (pleural, including empyema, pericardial, peritoneal); genitourinary (other antimicrobial therapy may be used simultaneously to control coincident urinary infection); skeletal (bony, articular, cartilaginous, synovial). | *inoperable*—several mo. to 1 yr.<br>*operable*—at least 3 wk. preoperatively and as long as needed postoperatively<br>*palliative*—1-2 wk. |
| adenitis; primary and secondary cutaneous; sinuses and fistulae; optic | *palliative*—only until desired result is achieved. For adenitis, until glands become impalpable or for 4 mo. |
| acute haematogenous disseminated (miliary); routine lumbar punctures should be done periodically to detect development of meningitis which often occurs with miliary tuberculosis | at least 1 yr. |

NON-TUBERCULOUS CONDITIONS

| *Conditions* | *Total Daily Dose** | *Treatment Duration* | *COMMENTS* |
|---|---|---|---|
| subacute bacterial endocarditis, penicillin-resistant | 2 Gm. (in divided doses q. 8-12 h.) | 3-4 wk. or longer depending on response | Perform *in vitro* tests for sensitivity periodically beginning before therapy. Supplementary penicillin or other antibiotic therapy may be necessary. |
| brucellosis, with bacteraemia | 1.5-3 Gm. (in divided doses q. 12 h.) | 14 days | In conjunction with a broad spectrum antibiotic such as tetracycline hydrochloride. |
| peritonitis due to gram-negative bacilli | 2-2.5 Gm. (in divided doses q. 8-12 h.) | 7-14 days | Supplementary penicillin and sulphonamide therapy may be necessary since bacterial flora is complex. |
| granuloma inguinale | 3 Gm. (in divided doses q. 12 h.) | 7-14 days | |
| urinary tract infections due to susceptible organisms | 1-2.5 Gm. (in divided doses q. 12 h.) | 5-7 days | Adequate surgical drainage and elimination of infective foci are essential. Severe infections may require the higher dosage for 14 days. Perform *in vitro* tests during treatment, particularly when the clinical response is slow or unsatisfactory. Local and constitutional symptoms may disappear without sterilization of urine. |
| acute gonorrhoea | 1 Gm. as a single injection, repeated if necessary | | Penicillin is drug of choice; give streptomycin only to those allergic or failing to respond to penicillin. Where concomitant syphilis is suspected, make darkfield examination before treatment and serologic tests monthly for 3 months. |

* *All dosages refer to mg. or Gm. equivalents of free base. Some other therapeutic agent should be added or substituted if streptomycin resistant strains occur.*

*Contraindications:* Streptomycin is contraindicated in those persons who have shown hypersensitivity to it.

*Precautions:* The caloric stimulation test for vestibular function and audiometric tests are advisable during prolonged streptomycin therapy to detect signs of developing eighth nerve damage: tests should be made before treatment is started and periodically thereafter. Vestibular damage may be permanent, although symptoms tend to disappear as the patient adjusts and learns to compensate visually. Auditory impairment is usually permanent.

As with any antibiotic preparation, prolonged use may result in an overgrowth of nonsusceptible organisms, including fungi. Constant observation of the patient is essential. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted.

*Adverse Reactions:* Streptomycin in sufficiently large doses may produce vestibular and auditory damage. There is evidence that streptomycin is less apt to produce auditory damage than is dihydrostreptomycin in comparable dosage. However, streptomycin is more apt to produce vestibular damage than is dihydrostreptomycin.

As with all products containing streptomycin, these products should be used with caution during pregnancy due to the potential hazard of ototoxicity to the foetus. Cases of vestibular and auditory damage to infants have been reported following treatment of the pregnant woman with streptomycin.

*Pre-existing renal impairment interferes with excretion, producing high blood levels and increasing the risk of toxicity from streptomycin and other anti-tuberculous agents. In the presence of pre-existing renal damage, the dosage of anti-tuberculous agents should be reduced to allow for drug retention; the blood concentration of streptomycin should not exceed 20 to 25 mcg./ml. plasma.*

Signs of kidney involvement (proteinuria, cylindruria, haematuria, and occasional azotaemia) generally disappear on withdrawal of the drug. Unless renal function is impaired, changes in the urine are usually not a cause for interrupting therapy. Pain and tenderness at the site of injection and skin eruptions may occur. Skin or other allergic reactions can usually be controlled with antihistaminics, but, if they persist, the drug should be withdrawn.

Headache, paraesthesias of the face and gastric disturbances may also occur. Clinical judgment as to termination of therapy must be exercised when such side effects occur.

*Directions for Reconstitution of the Sterile Powder:* Dilute with Sterile Water for Injection or Sodium Chloride Injection in the following manner: Loosen Powder. Hold vial horizontally and rotate it while *slowly* directing the stream of diluent against the wall of the vial. Shake vial vigorously after the diluent has been added.

Add 2 ml. or more diluent as desired to 0.75 Gm. vial.

The suggested maximum volume per injection is 2 ml. For a concentration of 250 mg./ml., add 3.7 ml. diluent to the 1 Gm. vial. For a concentration of 500 mg./ml., add 1.5 ml. to the 1 Gm. vial.

*Administration:* Streptomycin sulphate should be given *intramuscularly. Squibb Streptomycin Sulphate Injection should not be given intrathecally or intravenously because it contains a preservative.*

Intramuscular injections are sometimes painful, but pain is reduced if the following precautions are taken: (1) Inject high in the upper outer quadrant of the buttock. (2) Change the site for each injection. (3) Insert needle deeply to avoid subcutaneous deposition; inject slowly. *Use* 1% *procaine hydrochloride in distilled water as diluent for streptomycin sulphate powder, if necessary.*

Most authorities no longer recommend the intrathecal use of streptomycin for treating meningitis because of its toxicity when this route is employed and because the drug readily permeates inflamed meninges after intramuscular injection.

*Supply:* Vials containing equivalent of 0.75 Gm. and 1 Gm. streptomycin base. 0.75 Gm., boxes of 10 vials and 1 Gm., boxes of 25 vials.

*Expiration date* 39 months. Stable at room temperature. Sterile solutions freshly prepared from streptomycin powder may be kept at room temperature for 4 weeks without appreciable loss of potency. These solutions may become discoloured on standing, but this does not indicate any change which would prevent their use. Discoloration will be reduced materially or prevented if the solutions are refrigerated.

## ANATENSOL® — Tablets, Elixir

Squibb Fluphenazine Hydrochloride

Anatensol, Squibb Fluphenazine Hydrochloride, is a trifluoromethyl fluphenazine derivative intended for the management of anxiety and tension states, severe mental disorders, and behavioural problems in children. A highly potent behaviour modifier, Anatensol offers the advantage of a sustained and prolonged action.

Anatensol is available for oral administration as tablets and elixir. Anatensol Tablets are sugar-coated tablets of 1 mg. Anatensol Elixir is an orange-flavoured liquid providing 0.5 mg. per ml.

*Action:* Laboratory and clinical studies have demonstrated that while the pharmacologic effects of fluphenazine are, in general, similar to those of other phenothiazines, several important differences exist. First, fluphenazine is considerably more potent and has a more prolonged duration of action than either Siquil® (Squibb Triflupromazine Hydrochloride) or chlorpromazine. Second, because of its chemical structure, hypotension may be less likely to occur than with some of the older phenothiazine derivatives; nevertheless, appropriate caution should be observed, particularly with the higher dosage. See *Adverse Reactions and Precautions.* Third, fluphenazine appears to have less of a sedative effect than most other phenothiazines. It does not potentiate central nervous system depressants and anaesthetics to the same degree as some of the other phenothiazines. Moreover, in many psychotic patients, the drug seems to redirect the patient's activity rather than to suppress it.

Anatensol has undergone clinical trials in the treatment of various mental and

emotional disorders. In both acute and chronically ill psychotic patients, it has proved to be highly effective in modifying psychotic behaviour patterns and ameliorating such symptoms as agitation and delusions or hallucinations. The prolonged action of fluphenazine constitutes an outstanding advantage, permitting single daily administration of maintenance dosage in many patients.

Experimental and clinical studies suggest that the phenothiazine derivatives act on the hypothalamus; are believed to depress various components of the mesodiencephalic activating system, which is involved in the control of basal metabolism and body temperature, wakefulness, vasomotor tone, emesis, and hormonal balance; exert a peripheral autonomic effect in varying degrees. However, the site and mode of action of phenothiazine derivatives, including fluphenazine, have not been completely elucidated.

*Advantages:*

* sustained and prolonged action
* single daily dosage plan possible—optimal therapy for many patients
* maximal activity—most potent of available phenothiazines
* fewer toxic reactions than other phenothiazines
* side effects, including extrapyramidal symptoms, usually reversible by adjusting dosage to *lower therapeutic levels* and/or by using anti-Parkinsonism drugs
* effective in both acute and chronic patients
* strong antihallucinatory and antidelusional properties
* good patient acceptance—even in the elderly
* therapeutically effective without excessive sedation
* hypotension, if it occurs, rarely requires cessation of therapy
* maximum economy

*Indications:* Anatensol, in tablet and elixir forms, is of value in the alleviation of anxiety and tension complicating somatic disorders such as premenstrual tension, menopause, gastrointestinal disturbances, hypertension; environmental stress; tension headaches; emotional stress; psychoneurotic reactions; management of agitation and emotional instability in the aged; and in the management of behavioural problems in children.

Because of its marked ability to modify psychotic behaviour patterns, Anatensol is also of particular usefulness in the management of psychomotor agitation and overt hostility frequently associated with such acute and chronic psychoses as schizophrenia, mania, psychoses due to organic brain disease, mental deficiency, and senile psychoses.

*Contraindications:* Phenothiazines are contraindicated in patients with suspected or established subcortical brain damage, with or without hypothalamic damage, since a hyperthermic reaction with temperatures in excess of 104°F may occur, sometimes as late as 14 to 16 hours after drug administration, if the drug is used in such patients. If such a reaction should occur, total body ice-packing is recommended; anti-pyretics may also be useful.

Phenothiazine compounds should not be used in patients receiving large doses of hypnotics, and should be used with caution in patients with a history of convulsive disorders, since grand mal convulsions have been known to occur.

Patients with special medical disorders such as mitral insufficiency or phaeochromocytoma and patients who have exhibited idiosyncrasy to other centrally-acting drugs may experience severe reactions to phenothiazine compounds.

*Caution:* The use of phenothiazines as a class is associated with different degrees of drowsiness. Usually under the recommended dose, this is almost absent with fluphenazines. All the same, it is worthwhile to remember that engine crews, vehicle drivers and workers in workshops with fast moving parts, are advised not to use these drugs while on duty unless recommended and approved by the physician attending on them.

*Adverse Reactions and Precautions:* The most frequently reported side-effects associated with phenothiazine administration are reversible extra-pyramidal symptoms including Parkinsonism, dystonia, dyskinesia, akathisia, oculogyric crises, opisthotonos, and hyper-reflexia. Although these reactions may be alarming, all are reversible and disappear if dosage is lowered or therapy is temporarily discontinued. More rapid reversal may be achieved by administration of anti-Parkinsonian drugs or intravenous Caffeine and Sodium Benzoate Injection.

Liver damage as manifested by jaundice or biliary stasis may be encountered. Blood dyscrasias including leucopenia, agranulocytosis, thrombocytopenic purpura, eosinophilia, and pancytopenia have been observed with phenothiazine derivatives. For this reason, routine blood counts are advisable during therapy.

The patient should be observed for any soreness of the mouth, gums or throat or any symptoms of upper respiratory infection. If these symptoms occur and the confirmatory leucocyte count indicates cellular depression, therapy should be discontinued and other appropriate measures should be instituted immediately. Skin disorders such as itching, erythema, urticaria, and even exfoliative dermatitis have been reported with phenothiazine compounds. The possibility of anaphylactoid reactions occurring in some patients should be borne in mind.

Peripheral oedema, endocrine disturbances such as abnormal lactation, and autonomic reactions including nausea, anorexia, salivation, polyuria, perspiration, dry mouth, headache, and constipation may occur. Autonomic effects can usually be controlled by reducing or temporarily discontinuing dosage. Drowsiness or lethargy, if they occur, may necessitate a reduction in dosage; the induction of a catatonic-like state has been known to occur with dosages far in excess of the recommended amounts. As with other phenothiazine compounds, reactivation of psychotic processes may be encountered.

Hypotension is rarely a problem with fluphenazine; however, patients with pheochromocytoma, cerebral vascular or renal insufficiency, or a severe cardiac reserve deficiency such as mitral insufficiency appear to be particularly prone to hypotensive reactions with phenothiazine compounds and should be observed closely when the drug is administered. If severe hypotension should occur, supportive measures including the use of intravenous vasopressor drugs should be instituted immediately. Levarterenol Bitartrate Injection is the most suitable drug for this purpose; *epinephrine should not be used* since phenothiazine derivatives have been found to reverse its action, resulting in a further lowering of blood pressure. Psychotic patients on large doses of a phenothiazine drug who are

undergoing surgery should be watched carefully for possible hypotensive phenomena; reduced amounts of anaesthetics or central nervous system depressants may be required.

Although this is not a general feature of fluphenazine, potentiation of central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol) may occur. The effects of atropine may be potentiated in some patients receiving fluphenazine.

The following have never been reported with fluphenazine, although they have occurred with other phenothiazine derivatives: hypotension severe enough to cause fatal cardiac arrest, altered cerebrospinal fluid proteins, cerebral oedema, potentiation of phosphorus insecticides, photosensitivity, eczema, asthma, laryngeal oedema, angioneurotic oedema or pigmentary retinopathy.

*Overdosage:* See *Adverse Reactions and Precautions.* In the event of intentional or accidental overdosage, there is a possibility that dyskinetic manifestations, akathisia and Parkinsonism may appear, especially if the drug has been taken to excess over a period of days or weeks. Hypotension, blurred vision, dizziness or jitteriness may also occur.

Overdosage is treated symptomatically and supportively. If the patient is conscious, prompt gastric lavage, dilution of the stomach contents to delay absorption, or stimulation of vomiting should be attempted. In the conscious or unconscious patient an open airway should be maintained to preclude the possibility of respiratory difficulty. Drug-induced extra-pyramidal symptoms are generally amenable to anti-Parkinsonism drugs. In severe hypotension, the standard measures for management of circulatory shock should be instituted, e.g., vasoconstrictors and/or fluids administered intravenously. *l*-Norepinephrine bitartrate is recommended as a vasoconstrictive agent in this case.

*Administration and Dosage:*

*Anxiety and Tension States:* In anxiety and tension states, the suggested dosage for *adults* is 1 mg. both for initial and maintenance therapy, as a single dose. For severe conditions 1 mg. can be given twice daily to be followed by a maintenance dose of 1 mg. daily.

For *children* with situational, temporary or transient behavioural disorders of a mild degree, an initial dose of 0.25 mg. (0.5 ml. of elixir) or 0.5 mg. (1 ml. of elixir) daily is suggested. Dosage should be raised by increments of 0.25 mg. until symptoms are completely controlled. Doses larger than 1 mg. (2 ml. of elixir) should be used with caution.

*Mental Disorders in Adults:* Depending on severity and duration of symptoms, total daily dosage for *adult* psychotic patients may range initially from 2.5 to 10 mg. and should be divided and given at 6-to 8-hour intervals.

The smallest amount that will produce the desired results must be carefully determined for each individual, since optimal dosage levels of this potent drug vary from patient to patient. Treatment is best instituted with *low initial dosage*, which

may be increased, if necessary, until the desired clinical effects are achieved. Daily dosages exceeding 20 mg. should be used with caution. When symptoms are controlled, dosage can generally be reduced gradually to daily maintenance doses of 1 to 5 mg. often given as a single daily dose. Continued treatment is needed to achieve maximum therapeutic benefits; further adjustments in dosage may be necessary during the course of therapy to meet the patient's requirements.

For *geriatric* patients, the suggested starting dose is 1 to 2.5 mg. daily, adjusted according to the response of the patient.

*Mental Disorders and Behavioural Problems in Children:* In *children*, as well as adults, clinical experience has indicated that dosage varies with the individual. For psychotic children or children with behaviour disorders of psychotic proportions, a suggested dosage regimen of 1 mg. (2 ml. of elixir or 1 tablet of 1 mg.) once or twice daily and increasing up to a total daily dose of 3.5 mg. is generally adequate. Clinical reports have shown that a dosage as high as 10 mg. (20 ml. of elixir) daily has been used in some older children without untoward effects.

*Supply:* Sugar-coated tablets of 1.0 mg. in boxes of 100 (10 strips of 10's). Orange-flavoured elixir is available in 15 ml. and 30 ml. bottles with plastic dropper calibrated at 0.5 ml. and 1.0 ml.

## ANATENSOL® DECANOATE INJECTABLE — Parenteral Solution

Squibb Fluphenazine Decanoate Injection

Anatensol Decanoate is an esterified trifluoromethyl phenothiazine derivative. It is a highly potent antipsychotic agent with a markedly extended duration of action, available for intramuscular administration in 1 ml. vials providing 25 mg. fluphenazine decanoate in a sesame oil vehicle, with 1.2%(w/v) benzyl alcohol as a preservative.

*Indications :* Anatensol Decanoate is indicated in the management of psychotic disorders including schizophrenia, mania, and organic brain syndrome. It is of particular value in the treatment of chronic schizophrenia. The drug often alleviates such target symptoms as hallucinations, delusions, confusion, and withdrawal. It is not only useful in the hospital milieu but is unparalleled, because of its long duration of action, in the long-term maintenance therapy of chronically psychotic patients who are amenable to out-patient therapy.

*Medical Rationale :* The basic effects of fluphenazine decanoate appear to be no different from those of fluphenazine hydrochloride. The only exception to this is a prolonged duration of action. The esterification of fluphenazine with decanoic acid markedly prolongs the drug's duration of effect without reducing its activity. The onset of action generally appears between 24 and 72 hours after injection, and the effects of the drug on psychotic symptoms become significant within 49 to 96 hours. The therapeutic activity then continues for 1 to 4 weeks. To date Anatensol Decanoate is the longest-acting phenothiazine preparation available.

Like all phenothiazine derivatives, fluphenazine decanoate appears to act on the

hypothalamus, depressing various components of the mesodiencephalic activating system which is involved in the control of basal metabolism and body temperature, wakefulness, vasomotor tone, emesis, and hormonal balance. In addition, the phenothiazines exert a peripheral autonomic effect in varying degrees. However, the site and mode of action of the phenothiazines have not been completely elucidated.

Fluphenazine and its ester derivatives differ from other phenothiazines in several respects: fluphenazine and its esters are more potent on a milligram basis, appear to be less sedating, and have less potentiating effect on central nervous system depressants and anaesthetics than do some of the other phenothiazine derivatives; they are less likely than some of the older phenothiazines to produce hypotension.[1] (Nevertheless, appropriate cautions should be observed — see *Precautions* and *Adverse Reactions.*)

A long-acting parenteral antipsychotic agent is an invaluable aid both to the psychotic patient and to those who are responsible for him. Fluphenazine decanoate reduces hallucinations, delusions, confusion, withdrawal and, to a lesser degree, hostility and agitation. In general, the psychotic patient becomes more cooperative, less withdrawn, more responsive to social situations, and more subject to psychotherapy or other nonchemotherapeutic measures. In the hospital, the nursing staff is relieved of the need for daily or even more frequent administration of drugs to a class of patients who may be difficult to treat and who frequently dispose of oral medication without swallowing it. In out-patient care, where constant supervision is rarely feasible, the longer interval between injections reduces the problem of providing adequate maintenance dosage for patients who often fail to continue daily oral medication and consequently suffer frequent severe recurrences of acute psychotic episodes. Because maintenance medication can be more easily assured through the use of Anatensol Decanoate, it may be possible to release an increasing number of patients from custodial hospital care to an out-patient status.

Anatensol Decanoate produces far fewer extrapyramidal side effects and a larger proportion of milder extrapyramidal side effects than any other fluphenazine product. A study conducted to determine the effects of Anatensol Decanoate revealed that out of 501 patients 314 (62.7%) did not exhibit any extrapyramidal side effects. Out of the 187 patients who did show a variety of extrapyramidal side effects, 94 (50%) exhibited symptoms of only mild severity.

*Adverse Effects : Central Nervous System.* The side effects most frequently reported with phenothiazine compounds and other antipsychotic agents are extrapyramidal symptoms such as pseudo-Parkinsonian (tremor, rigidity, etc.), akathisia. They are *usually reversible*: however, a persistent pseudo-Parkinsonian syndrome may develop after prolonged administration of phenothiazines. This syndrome is characterized by rhythmic, stereotyped, dyskinetic, involuntary movements (particularly of the face, mouth, tongue and jaw ) which resemble the facial grimaces of encephalitis. These may be accompanied by choreiform movements of the limbs. In these chronic cases, the symptoms may persist after drug withdrawal, and appear to be irreversible in some patients. Anti-Parkinsonian agents may not be of benefit in these instances. The risk of developing

this persistent syndrome appears to be greatest in elderly female patients with organic brain disease or damage who have been receiving fairly large doses of phenothiazines for a prolonged period.

Extrapyramidal reactions may be alarming and the patient should be forewarned and reassured. These reactions can usually be controlled by administration of anti-Parkinsonian drugs and, if necessary, reduction in dosage.

A reduction in dosage or symptomatic treatment may be necessary to relieve drowsiness, lethargy, or depression, if they occur. As with other phenothiazines, reactivation or aggravation of psychotic processes may be encountered. Phenothiazine derivatives have been known to cause restlessness, excitement or bizarre dreams in some patients.

*Autonomic Nervous System.* Hypotension has rarely presented a problem with fluphenazines. However, patients with pheochromocytoma, cerebral vascular or renal insufficiency, or a severe cardiac reserve deficiency such as may occur in mitral insufficiency, appear to be particularly prone to hypotensive reactions with phenothiazines; they should, therefore, be observed closely when the drug is administered. If severe hypotension should occur, supportive measures including the use of intravenous vasopressor drugs should be instituted immediately. Levarterenol Bitartrate U.S.P. (Levophed) is the most suitable drug for this purpose: *epinephrine should not be used* since phenothiazine derivatives have been found to reverse its action, further lowering the blood pressure.

Hypertension and fluctuations in blood pressure have been reported with phenothiazines.

Autonomic reactions including nausea and loss of appetite, salivation, polyuria, perspiration, dry mouth, headache, and constipation may occur. Autonomic effects can usually be controlled by reducing or temporarily interrupting dosage. In some patients, phenothiazine derivatives have caused blurred vision, glaucoma, bladder paralysis, faecal impaction, paralytic ileus, tachycardia, or nasal congestion.

*Metabolism and Endocrine System.* Weight change, peripheral oedema, abnormal lactation, gynaecomastia, menstrual irregularities, false results on pregnancy tests, impotency in men, and increased libido in women have all been known to occur in some patients on phenothiazine therapy.

*Allergic reactions.* Skin disorders such as itching, erythema, urticaria, seborrhoea, photosensitivity, eczema and even exfoliative dermatitis have been reported with phenothiazine derivatives.

*Other reactions.* Sudden, unexpected, and unexplained deaths have been reported in hospitalized psychotic patients receiving phenothiazines. Previous brain damage or seizures may be predisposing factors; high doses should be avoided in known seizure patients.[2] Several patients have shown sudden flare-ups of psychotic behaviour patterns shortly before death. Autopsy findings in these cases have usually revealed acute fulminating pneumonia or pneumonitis, aspiration of gastric contents, or intramyocardial lesions.[2,4,5]

Although this is not a general feature of fluphenazine, potentiation of central nervous system depressants (opiates, analgesics, antihistamines, barbiturates, alcohol) may occur — see *Precautions* for patients undergoing surgery. The effects of atropine may also be potentiated in some patients.

The following adverse reactions have also occurred with phenothiazine derivatives: hypotension severe enough to cause fatal cardiac arrest, altered electrocardiographic and electroencephalographic tracings, altered cerebrospinal fluid proteins, cerebral oedema, disturbances of body temperature (hypo- and hyperthermia), potentiation of reactions to extreme heat, potentiation of reactions to phosphorus insecticides, asthma, laryngeal oedema, angioneurotic oedema and pigmentary retinopathy; with long-term use, skin pigmentation and lenticular and corneal opacities have also occurred.

Injections of fluphenazine decanoate are extremely well tolerated, local tissue reactions occurring only rarely.

*Precautions:* Fluphenazine decanoate should be used cautiously in patients who have had cholestatic jaundice. Liver damage rarely manifested by cholestatic jaundice may be encountered during therapy.[2] Treatment should be discontinued if this occurs. Alterations in cephalin flocculation or alkaline phosphatase and/or increased thymol turbidity (with or without leucocytosis) sometimes accompanied by abnormalities in other liver function tests, have been reported in patients receiving fluphenazine decanoate who have had no clinical evidence of liver damage. This, however, is not uncommon with phenothiazine therapy.[3]

Renal function of patients on long-term therapy should be monitored; if BUN (Blood Urea Nitrogen) becomes abnormal, treatment may have to be discontinued.

Routine blood counts are advisable during therapy since rare instances of blood dyscrasias including leucopenia, agranulocytosis, thrombocytopenic or non-thrombocytopenic purpura, eosinophilia, and pancytopenia have been reported with some phenothiazine derivatives. If any soreness of the mouth, gums, or throat, or any symptoms of upper respiratory infection occur and a leucocyte count confirms cellular depression, therapy should be discontinued and appropriate measures instituted immediately.

Phenothiazine should be used with caution in patients with a history of convulsive disorders, since grand mal convulsions have been known to occur.

Patients with special medical disorders such as mitral insufficiency or pheochromocytoma, and patients who have exhibited idiosyncrasy to other centrally-acting drugs may experience severe reactions to phenothiazine compounds.

Anaphylactoid reactions may occur in some patients. Fluphenazine decanoate should be used cautiously in patients with a history of skin rashes or other allergic reactions to another phenothiazine compound because of the possibility of cross-sensitivity.

*When undergoing surgery.* Psychotic patients receiving large doses of a phenothiazine preparation should be watched carefully for possible hypotensive phenomena. Moreover, it should be remembered that a reduction in dosage of anaesthetics or central nervous system depressants may be required.

As with any phenothiazine, the physician should be alert to the possible development of "silent pneumonias" in patients under treatment with fluphenazine decanoate.

Fluphenazine decanoate should be administered under the direction of a physician experienced in the clinical use of psychotropic drugs, particularly phenothiazine derivatives. Furthermore, facilities should be available for periodic checking of the hepatic function, renal function, and the blood picture.

*Contraindications:* Phenothiazines are contraindicated in patients with suspected or established subcortical brain damage, with or without hypothalamic damage, since a hyperthermic reaction with temperatures in excess of 104°F may occur in such patients. Sometimes this reaction may not occur until 14 to 16 hours after drug administration. If it does occur, total body ice-packing is recommended; antipyretics may also be useful.

Phenothiazine should not be used in patients receiving large doses of hypnotics (see *Precautions* for patients undergoing surgery).

As with other phenothiazines, Anatensol Decanoate Injectable (Squibb Fluphenazine Decanoate Injection) is contraindicated in comatose or severely depressed states.

The presence of blood dyscrasia, liver disease, or renal insufficiency precludes the use of fluphenazine decanoate.

Fluphenazine decanoate is not intended for use in children under 12 years of age.

*Administration and Dosage : The usual adequate dosage* of fluphenazine decanoate is 25 mg. (1 ml.) every 3 to 4 weeks. If necessary, adjustments in the amount and the dosage interval may be made in accordance with the patient's response.

The optimal amount of the drug and the frequency of administration must be determined for each patient, since dosage requirements have been found to vary with clinical circumstances as well as with individual response to the drug. Although in a large series of patients the optimal dose was usually 25 mg. (1 ml.) every 3 to 4 weeks, the amount required ranged from 12.5 to 75 mg. (0.5 to 3 ml.). The interval between doses ranged from 2 weeks to 5 weeks in most instances but some patients required doses as often as once every 3 days for the first few injections, while the response to a single dose was found to last 6 weeks or longer in a few patients on maintenance therapy.

For *patients who have had no previous therapy*, it is advisable to initiate treatment with an oral antipsychotic agent such as Anatensol Tablets (Squibb Fluphenazine Hydrochloride) — see package insert accompanying this product for complete information. When optimal response has been established,

fluphenazine decanoate should be administered at 25 mg. (1 ml.) every 3 to 4 weeks. In switching over to fluphenazine decanoate, the quick-acting antipsychotic agent should be administered concurrently for 3 days, and then discontinued.

For *patients on short-acting phenothiazine drugs*, fluphenazine decanoate at 25 mg. (1 ml.) every 3 to 4 weeks should be adequate. The previous antipsychotic agent should be administered concurrently for 3 days, and then discontinued.

For *patients on fluphenazine enanthate therapy*, the equivalent dosage of fluphenazine decanoate will provide longer interval between administrations.

*"Poor risk" patients* (those with known hypersensitivity to phenothiazine, or with disorders that predispose to undue reactions): therapy should be initiated cautiously with a quick-acting oral antipsychotic agent (such as fluphenazine hydrochloride — see package insert accompanying product for complete information). When optimal response has been established, fluphenazine decanoate should be administered at 25 mg. (1 ml.) every three weeks. In switching over to fluphenazine decanoate, the quick-acting antipsychotic agent should be administered concurrently for 3 days, and then discontinued.

*Supply:* Anatensol Decanoate Injectable is supplied in 1 ml. vials providing 25 mg. fluphenazine decanoate.

*Note :* Anatensol Decanoate Injectable should be administered intramuscularly. A dry needle and syringe should be used. Use of a wet needle or syringe may cause the solution to become cloudy. Store in a cool, dark place.

*Expiration date* 18 months.

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*References:*

1. Himwich, H.: Comparative values of phenothiazine drugs. Presented before the American Psychiatric Association Regional Research Conference, Little Rock, Ark., February 1959.
2. Hollister, L. E.: Adverse Reactions to Phenothiazines. J. A. M. A. 189:311 (1964).
3. Bloom, J. B., *et al.*: Effect on the Liver of Long-Term Tranquilizing Medication. Am. J. Psychiat. 121:788 (1965).
4. Lapolla, A., and Nash, L. R.: Sudden Death in Mental Institutions. Presented before the American Psychiatric Association Western Meeting, Hawaii, Aug. 1965.
5. Richardson, H. L., *et al.*: Intramyocardial Lesions in Patients Dying suddenly and unexpectedly. J.A.M.A. 195:254 (1966).

## ANATENSOL® ENANTHATE INJECTABLE — Parenteral Solution

Squibb Fluphenazine Enanthate

Anatensol Enanthate Injectable (Squibb Fluphenazine Enanthate) is an esterified trifluoromethyl phenothiazine derivative, chemically designated as 4-3-2 (Tri-

fluoromethyl)-phenothiazine-10-yl propyl-l-piperazine-ethanol heptanoate(enanthate). It is a highly potent and anti-psychotic agent with a markedly extended duration of effect, available for parenteral administration in vials providing 25 mg. fluphenazine enanthate per ml. in a sesame oil vehicle, with 1.5% benzyl alcohol as a preservative.

*Action:* Phenothiazine derivatives appear to act on the hypothalamus, depressing various components of the mesodiencephalic activating system. In addition, the drugs exert a peripheral autonomic effect in varying degrees. However, the site and mode of action of the phenothiazine derivatives have not been completely elucidated.

In the treatment of psychotic disorders, fluphenazine alleviates many of the psychotic symptoms. The drug is primarily effective in reducing hostility, anxiety, agitation and hyperactivity. In general, the psychotic patient becomes more cooperative, more responsive to social situations, and more subject to basic therapy.

Fluphenazine differs from the other phenothiazine derivatives in several respects; it is more potent on a milligram to milligram basis, it has a potentiating effect on central nervous system depressants and anaesthetics than do some of the phenothiazines and appears to be less sedating, and it is less likely than some of the older phenothiazines to produce hypotension (nevertheless, appropriate cautions should be observed—see section on *Side Effects and Precautions*).

The esterification of fluphenazine markedly prolongs the drug's duration of effect without unduly extenuating its beneficial action. The onset of action generally appears between 24 to 72 hours after injection, and the effects of the drug on psychotic symptoms become significant within 48 to 96 hours. Amelioration of symptoms then continues for 1 to 3 weeks or longer, with an average duration of effect of about 2 weeks.

A long-acting parenteral behaviour modifier provides several advantages in the treatment of psychotic patients. In hospital, the nursing staff is relieved of the need for daily or even more frequent administration of drugs to a class of patients who, by the nature of their disorder, may be difficult to treat, and who frequently dispose of oral medication without swallowing it. In out-patient care, where constant supervision is rarely feasible, a bi-weekly injection reduces the problem of providing adequate maintenance dosage for possibly erratic patients who often fail to continue with daily oral medication and consequently suffer frequent severe recurrence of acute psychotic episodes. Because maintenance medication can be more easily assured through the use of Anatensol Enanthate Injectable (Squibb Fluphenazine Enanthate), it may be possible to release an increasing number of patients from custodial hospital care to an out-patient status.

*Indications:* Anatensol Enanthate Injectable (Squibb Fluphenazine Enanthate) is indicated principally in schizophrenia, mania, and organic brain disease. The drug alleviates such symptoms as agitation, hostility, and anxiety which are often associated with psychoses. Anatensol Enanthate Injectable (Squibb Fluphenazine Enanthate) finds useful application not only in the hospital milieu, but also in the long term maintenance therapy of chronically psychotic patients who are treatable on an out-patient basis.

*Contraindications:* Phenothiazines are contraindicated in patients with suspected or established subcortical brain damage, with or without hypothalamic damage, since a hyperthermic reaction with temperatures in excess of 104°F may occur in such patients, sometimes not until 14 to 16 hours after drug administration. Total body ice-packing is recommended for such a reaction; antipyretics may also be useful. Phenothiazine compounds should not be used in patients receiving large doses of hypnotics, and should be used with caution in patients with a history of convulsive disorders, since grand mal convulsions have been known to occur.

Patients with special medical disorders such as mitral insufficiency or pheochromocytoma and patients who have exhibited idiosyncrasy to other centrally acting drugs may experience severe reactions to phenothiazine compounds. Fluphenazine enanthate is not intended for use in children under 12 years of age.

*Side Effects and Precautions:* The most frequently reported side effects associated with phenothiazine administration are reversible extra-pyramidal symptoms including Parkinsonism, dystonia, dyskinesia, akathisia, oculogyric crises, opisthotonos, and hyper-reflexia. Although these reactions may be alarming, all are reversible and can usually be controlled by administration of anti-Parkinsonian drugs such as Tri-hexyphenidyl hydrochloride or intravenous Caffeine and Sodium Benzoate Injection, and by subsequent reduction in dosage.

Liver damage as manifested by jaundice or biliary stasis may be encountered. Blood dyscrasias including leucopenia, agranulocytosis, thrombocytopenic purpura, eosinophilia, and pancytopenia have been observed with phenothiazine derivatives. For this reason, routine blood counts are advisable during therapy. The patient should be observed for any soreness of the mouth, gums or throat or any symptoms of upper respiratory infection. If these symptoms occur and confirmatory leucocyte count indicates cellular depression, therapy should be discontinued and other appropriate measures should be instituted immediately.

Peripheral oedema, endocrine disturbances such as abnormal lactation, and autonomic reactions including nausea and loss of appetite, salivation, polyuria, perspiration, dry mouth, headache, and constipation may occur. Autonomic effects can usually be controlled by reducing or temporarily discontinuing dosage. Drowsiness or lethargy, if they occur, may necessitate a reduction in dosage; the induction of a catatonic-like state has been known to occur with dosages far in excess of the recommended amounts.

Hypertension and fluctuations in blood pressure have been reported with fluphenazine enanthate. Hypotension has rarely presented a problem with fluphenazine. However, patients with pheochromocytoma, cerebral, vascular or renal insufficiency, or a severe cardiac reserve deficiency such as mitral insufficiency appear to be particularly prone to hypotensive reactions with phenothiazine compounds, and should therefore be observed closely when the drug is administered. If severe hypotension should occur, supportive measures including the use of intravenous vasopressor drugs should be instituted immediately. Levarterenol Bitartrate (Levophed) is the most suitable drug for this purpose: *epinephrine should not be used* since phenothiazine derivatives have been found to reverse its action, resulting in a further lowering of blood pressure. Psychotic patients on large doses of phenothiazine drug who are undergoing surgery should be watched carefully for possible hypotensive phenomena. Moreover,

it should be remembered that reduced amounts of anaesthetics or central nervous system depressants may be required.

Although this is not a general feature of fluphenazine, potentiation of central nervous system depressants (opiates, analgesics, anti-histamines, barbiturates, alcohol) may occur. The effects of atropine may be potentiated in some patients receiving fluphenazine.

Renal function of patients on long-term therapy should be monitored; if BUN (Blood Urea Nitrogen) becomes abnormal, treatment should be discontinued.

Autonomic reactions including nausea and loss of appetite, salivation, polyuria, perspiration, dry mouth, headache, and constipation may occur. Autonomic effects can usually be controlled by reducing or temporarily discontinuing dosage.

*Allergic Reactions:* Skin disorders such as itching, erythema, urticaria, seborrhoea, photosensitivity, eczema and even exfoliative dermatitis have been reported with phenothiazine derivatives. The possibility of anaphylactoid reactions occurring in some patients should be borne in mind.

*Others:* Sudden, unexpected and unexplained deaths have been reported in hospitalized psychotic patients receiving phenothiazines. Previous brain damage or seizures may be predisposing factors, high doses should be avoided in known seizure patients. Several patients have shown sudden flare-ups of psychotic behaviour patterns shortly before death. Autopsy findings have usually revealed acute fulminating pneumonia or pneumonitis, aspiration of gastric contents, or intra-myocardial lesions.

The following adverse reactions have also occurred with phenothiazine derivatives, hypotension severe enough to cause fatal cardiac arrest, altered electrocardiographic and electroencephalographic tracings, altered cerebrospinal fluid proteins, cerebral oedema, potentiation of heat and of phosphorus insecticides, asthma, laryngeal oedema, angioneurotic oedema, and pigmentary retinopathy, with long-term use—skin pigmentation, and lenticular and corneal opacities.

Injection of fluphenazine enanthate is extremely well tolerated, local tissue reactions occurring only rarely.

*Dosage:* The usual dose of Anatensol Enanthate Injectable (Squibb Fluphenazine Enanthate) is 25 mg. (1 ml.) every two weeks, given intramuscularly or subcutaneously. Individual dose requirements vary, however, and may range from 12.5 to 100 mg. (0.5 to 4 ml.) given at intervals of 1 to 3 weeks. The amount and frequency of dosage should therefore be adjusted in accordance with patient response.

Anatensol Enanthate Injectable (Squibb Fluphenazine Enanthate) may be given for initial as well as for maintenance therapy.

*Supply:* Anatensol Enanthate Injectable is supplied as multiple dose in 2 ml. vials.

*Note:* A dry needle and syringe should be used. Use of a wet needle or syringe may cause the solution to become cloudy. Store in a cool, dark place.

*Expiration date* 18 months.

## ASCORBICIN®

**Tablets**

Squibb Ascorbic Acid—Vitamin C

Ascorbicin is Squibb Ascorbic Acid (Vitamin C).

In the body, vitamin C plays the role of general activator of metabolic processes. In particular it regulates intracellular respiration and metabolism, stimulates the maturation of elements of the blood (erythrocytes, leucocytes and thrombocytes), the formation of interstitial substance (collagenous fibres of the connective tissue, dentine, ossein) and defence mechanisms against infections and intoxications (by inactivation of toxins, formation of antibodies and alexins).

*Indications:* Ascorbicin is indicated in the treatment of vitamin C deficiency. Ascorbicin is also indicated for the prevention or treatment of scurvy or where there is a pathologic interference with its assimilation in amounts necessary for the preservation of health. Ascorbicin is also of value where dental caries, pyorrhoea, gum infections, anorexia, anaemia, under-nutrition, increased capillary fragility or other conditions result from a deficiency of vitamin C. Given before and after surgery, Ascorbicin aids in the healing of wounds in patients with clinical or subclinical vitamin C deficiency.

*Dosage:* Orally: 1 or more tablets daily as directed by the physician.

*Supply:* Yellow press-coated tablets of 250 mg., bottles of 20 and 100.

*Expiration date* 24 months.

## AVEDAN®

**Tablets**

Squibb Analgesic Compound

Avedan is a rapid-acting analgesic and antipyretic compound containing in addition to aspirin and caffeine, N-acetyl-p-aminophenol (acetaminophen), the chief active metabolite of acetanilid and acetophenetidin. Each Avedan tablet contains 0.125 Gm. (2 gr.) acetaminophen, 0.23 Gm. (3½ gr.) aspirin, and 0.03 Gm. (½ gr.) caffeine.

*Advantages:* With two Avedan tablets there is a marked rise in the pain threshold within 30 minutes, with a peak effect in about 2½ hours—analgesia is maintained for about 4 hours. Avedan is nonaddicting.

*Indications:* Avedan is particularly useful for fast temporary relief of neuralgic and musculoskeletal pain; more specifically, for pain in such conditions as simple headache, migraine, dysmenorrhoea, common colds and grippe, myalgias, neuralgia, bursitis, sinusitis, and after dental extractions and minor surgery.

*Precautions:* Avedan should not be used for more than 10 days and should not be administered to children under 6 years unless directed by the physician. Keep it out of the reach of children.

*Dosage:* Adults, 1 or 2 tablets with water. May be repeated every 2 hours but not to exceed 12 tablets in 24 hours.

*Supply:* Boxes of 100 tablets (10 strips of 10's).

## AVEDAN® PLUS — Tablets

Squibb Analgesic Compound

Each Tablet of Avedan Plus contains:

| | |
|---|---|
| Acetyl-p-aminophenol N.F. | 0.125 Gm. |
| Aspirin I.P. | 0.350 Gm. |
| Caffeine I.P. | 30 mg. |

*Advantages:* Avedan Plus is a rapidly acting analgesic and antipyretic compound containing in addition to aspirin and caffeine a strong and safe analgesic Acetyl-p-aminophenol. With oral administration of one tablet of Avedan Plus there is marked rise in the pain threshold within 30 minutes and reaches its peak in about 2½ hours. Its effect is maintained for about 4 hours.

*Indications:* Avedan Plus is a strong analgesic particularly useful for fast temporary relief of neuralgic and musculoskeletal pain; more specifically, for pain in such conditions as simple headache, migraine, dysmenorrhoea, common colds and grippe, myalgias, neuralgia, bursitis, sinusitis, after dental extractions and minor surgery.

*Precautions:* Avedan Plus should not be used for more than 10 days and should not be administered to children under 6 years unless directed by the physician. Keep out of the reach of children.

*Dosage:* Adults, 1 or 2 tablets with water. May be repeated every 2 hours but not to exceed 12 tablets in 24 hours.

*Supply:* Boxes of 100 tablets (10 strips of 10's).

## BASITON® — Capsules

Squibb B Complex Vitamins, Yeast, Folic Acid and Vitamin $B_{12}$

Basiton Capsules contain important B Complex Vitamins plus Yeast, Folic Acid and Vitamin $B_{12}$ for oral administration. The administration of a vitamin supplement containing the B Complex Vitamins, including Vitamin $B_{12}$, helps assure more effective protection against B Complex deficiencies.

Each Basiton Capsule contains:

| | |
|---|---|
| Vitamin $B_1$ (Thiamine Mononitrate) | 2.0 mg. |
| Vitamin $B_2$ (Riboflavine) | 2.0 mg. |
| Niacinamide | 15.0 mg. |
| Vitamin $B_6$ (Pyridoxine Hydrochloride) | 0.125 mg. |
| Calcium Pantothenate | 2.0 mg. |
| Brewers' Yeast (1½ gr.) | 100.0 mg. |

| | |
|---|---|
| Vitamin $B_{12}$ | 2.0 mcg. |
| Folic Acid | 0.134 mg. |

*Indications:* Basiton Capsules as a dietary supplement, are useful in guarding against deficiencies of B Complex Vitamins in persons who do not or cannot consume adequate diets.

*Dosage:* One to four capsules daily.

*Supply:* Bottles of 25 and 100 capsules.

*Note:* Keep away from excessive heat.

*Expiration date* 24 months.

## BASITON® FORTE INJECTION

**Parenteral Solution**

Squibb Stress B Complex Vitamins

Basiton Forte Injection is Squibb Stress B Complex Vitamins for intramuscular use. It contains seven physiologically important and therapeutically useful members of the B Complex vitamins and provides high potency B Complex therapy. Basiton Forte Injection is available as a special pack wherein the Vitamin $B_{12}$ is given separately in an ampoule. Before use the contents of the ampoule have to be added to the vial to give a total volume of 5 ml.

Each ml. of the reconstituted solution supplies:

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|---|---|
| Vitamin $B_{12}$ (Cyanocobalamin) | 50 mcg. |
| Vitamin $B_1$ (Thiamine Hydrochloride) | 50 mg. |
| Vitamin $B_2$ (Riboflavine) | 5 mg. |
| Niacinamide | 100 mg. |
| Vitamin $B_6$ (Pyridoxine Hydrochloride) | 5 mg. |
| Panthenol | 5 mg. |
| Choline (as chloride) | 25 mg. |

*Indications:* Basiton Forte Injection contains all the major factors of vitamin B Complex in therapeutic amounts; it is useful for the vitamin B Complex deficiency states met with in clinical practice. Deficiency of a single factor of B Complex is relatively rare without a latent deficiency of other B Complex factors also. Hence Basiton Forte Injection is indicated for the treatment of vitamin B Complex deficiencies. These can be manifested as glossitis, stomatitis, ulcers of the mucous membranes of mouth, cheilosis, conjunctivitis, photophobia, epiphora, scleral injection, vomiting, anorexia, diarrhoea, neuritis, paraesthesias, tenderness of calf muscles, weakness, fatigue, vague neuritic pain, pellagrous dermatitis, burning foot syndrome, etc. It is also useful in debility during convalescence, vitamin B Complex deficiency due to broad spectrum antibiotic therapy, chronic debilitating diseases and diabetes mellitus.

Administration of Basiton Forte Injection provides for the increased requirements of vitamin accompanying alcoholism, thyrotoxicosis, serious illness or tissue damage caused by injury, burns, excessive radiation or surgery. Post-

operatively, Basiton Forte Injection therapy is recommended in the presence of anorexia or vomiting, particularly for patients receiving infusions of saline or glucose as such infusions may cause rapid depletion of water-soluble vitamins by increasing their rate of urinary excretion. Moreover, many of the B complex vitamins form enzymes essential for the oxidation of glucose and infusions of glucose solutions may deplete tissue stores of B vitamins. Since B vitamins are also concerned with protein and amino acid metabolism, liberal quantities of the vitamin B Complex should be given to patients receiving amino acid or protein preparations parenterally.

Basiton Forte Injection is specially indicated in severe B Complex deficiencies, particularly in patients who cannot tolerate oral medication or in whom there is evidence of poor gastrointestinal absorption.

*Advantages:*

* contains seven physiologically important and therapeutically useful members of B Complex in high potency
* combats even severe B Complex deficiencies, particularly in patients who cannot tolerate oral medication or in whom there is evidence of poor gastrointestinal absorption
* available as a special pack wherein the vitamin $B_{12}$ is given separately in an ampoule

*Administration and Dosage:* Before use inject the contents of the ampoule into the vial and mix properly. One ml. intramuscularly, once or twice a day as may be decided by the physician.

Reconstituted solution should be used up during the period required to complete the recommended course of injection.

*Supply:* Basiton Forte Injection is available as a special pack wherein the vitamin $B_{12}$ is given separately in an ampoule. Before use, the contents of the ampoule have to be added to the vial to give a total volume of 5 ml.

*Expiration date* 12 months.

## BASITON® FORTE — Tablets

Squibb Vitamin B Complex with Vitamin C

Basiton Forte Tablets, Squibb Vitamin B Complex with Vitamin C for oral use, supply high dosage of all essential B Complex vitamins including folic acid and vitamin $B_{12}$; in addition Basiton Forte Tablets also contain therapeutic dosage of vitamin C.

Each Basiton Forte Tablet contains:

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|---|---|
| Vitamin $B_1$ (Thiamine Mononitrate) | 10 mg. |
| Vitamin $B_2$ (Riboflavine) | 10 mg. |
| Vitamin $B_6$ (Pyridoxine Hydrochloride) | 2 mg. |

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|---|---|
| Niacinamide | 100 mg. |
| Calcium Pantothenate | 50 mg. |
| Vitamin $B_{12}$ (Cyanocobalamin) | 4 mcg. |
| Vitamin C (as Sodium Ascorbate) | 300 mg. |
| Folic Acid | 1.5 mg. |

*Indications:* Basiton Forte Tablets contain all the major water soluble vitamins. Basiton Forte Tablets are not only useful for prophylaxis and treatment of vitamin B Complex deficiencies but also for the prevention and treatment of concurrent vitamin C deficiency. Basiton Forte Tablets are specially useful whenever stress formula vitamins are indicated; as after broad spectrum antibiotic therapy, chronic debilitating diseases, diabetes mellitus, hepatic diseases, pregnancy and lactation, fractures and chronic alcoholism. The symptoms of water soluble vitamin deficiencies are often seen in acute or chronic malnutrition, post-operatively and during and after convalescence. These symptoms can be manifested as glossitis, stomatitis, ulcers of the mucous membranes of mouth, cheilosis, conjunctivitis, photophobia, epiphora, scleral injection, vomiting, anorexia, diarrhoea, neuritis, paraesthesias, tenderness of calf muscles, weakness, fatigue, vague neuritic pain, pellagrous dermatitis, burning foot syndrome and bleeding gums, etc. Basiton Forte Tablets may be prescribed for any of these symptoms.

*Advantages:*

* high potency B Complex and vitamin C in Basiton Forte Tablets help overcome even severe physiologic drain
* helps overcome nutritional deficiency

*Dosage: For prophylaxis as well as treatment*—one tablet a day is usually sufficient. *In severe deficiencies*—one or more tablets a day, as decided by the physician.

*Supply:* Basiton Forte Tablets are supplied in boxes of 100 tablets (10 strips of 10's).

*Expiration date* 18 months.

## BELAMYL®

**Parenteral Solution**

Squibb B Complex Liver Extract with Vitamin $B_{12}$

Belamyl supplies Squibb B Complex Liver Extract—a source of the whole, natural B Complex of Liver, with all the anti-anaemia factors present. Since the effectiveness of crude liver has been repeatedly demonstrated, the liver extract in Belamyl is in as crude a form as consistent with safe parenteral administration. To the liver extract of Belamyl have been added therapeutic amounts of Vitamin $B_{12}$—the most potent anti-anaemia substance known—and thiamine, riboflavine and niacinamide—essential B Complex vitamins.

Each 1 ml. of Belamyl supplies 0.66 ml. Crude Liver Extract equivalent to 1.33 mcg. Vitamin $B_{12}$ *activity* fortified with:

| | |
|---|---|
| Vitamin $B_{12}$ *Crystalline* | 10 mcg. |
| Thiamine Hydrochloride | 10 mg. |

| | |
|---|---|
| Riboflavine | 3 mg. |
| Niacinamide | 100 mg. |

*Indications:* Belamyl is indicated in vitamin B Complex deficiency states and in severe nutritive failure. It may also be used therapeutically or adjunctively in beri-beri, ariboflavinosis and pellagra, both clinical and subclinical. It may also be of value in tropical and nutritional macrocytic anaemias, the sprue syndrome and in pernicious anaemia.

*Advantages:* Four important advantages to the clinician are offered in each single injection of Belamyl:

1. A therapeutic dose of the natural B Complex as it occurs in mammalian liver.
2. A therapeutic dose of Vitamin $B_{12}$—one of the most potent anti-anaemia substances known.
3. A therapeutic dose of three other critical vitamin B Complex factors.
4. Parenteral administration to assure absorption.

*Administration:* Belamyl is given by deep intramuscular injection into the upper outer quadrant of the buttock.

*Dosage:* Dosage depends on the condition being treated, the average dose being 1 ml. given 1 to 3 times a week. In the treatment of pernicious anaemia, particularly in the presence of neurologic symptoms a dose of 1 ml. tri-weekly is suggested. When remission of symptoms occurs, a maintenance dose of 1 ml. per week may be advisable. For the initial treatment of pernicious anaemia, Belamyl is to be used in addition to Rubramin® therapy. In the presence of neurologic symptoms large supplementary doses of Rubramin or Rubramin-H are required.

*Supply:* Vials of 5 ml.

*Note:* Belamyl should be kept in a cool place and away from exposure to sunlight.

*Expiration date* 24 months.

## CARBOTUSS®

**Tablets**

Squibb Cold Tablets

Carbotuss Tablets (Squibb Cold Tablets) contain an effective combination of well-established drugs for the treatment and symptomatic relief of the common cold.

Each Carbotuss Tablet contains:

| | |
|---|---|
| Acetyl-p-Aminophenol | 250 mg. |
| Noscapine | 10 mg. |

| | |
|---|---|
| Phenylephrine Hydrochloride | 5 mg. |
| Carbinoxamine Maleate | 1.2 mg. |
| Vitamin C (in the form of Sodium Ascorbate) | 20 mg. |

*Action:* Acetyl-p-Aminophenol, the active metabolite of acetanilide and acetophenetidin is a non-narcotic, non-addicting, well established analgesic agent. Acetyl-p-Aminophenol is rapidly absorbed from the gastrointestinal tract of rats and enters into most cells of the body with uniform distribution; there is no evidence of appreciable concentrations in any one tissue. Acetyl-p-Aminophenol does not cause methaemoglobinaemia and it is rapidly eliminated in the urine, in small part in the free form, but mainly in conjugation with sulphuric or glucuronic acid.

Noscapine is an effective, non-narcotic, non-addicting cough suppressant drug and is equal to codeine in its anti-tussive effect. The exact mechanism by which noscapine suppresses the cough reflex is not known. None of the unpleasant side effects of codeine, e.g., constipation, miosis, blood pressure changes, or respiratory depression were observed after noscapine administration. Noscapine's action on smooth muscle resembles that of papaverine, inducing bronchodilatation with much larger than therapeutic doses. Phenylephrine hydrochloride, a synthetic sympathomimetic amine closely resembles epinephrine and ephedrine in its pharmacological action, particularly in its ability to relieve the nasal congestion of colds and allergy. In man, phenylephrine hydrochloride causes less nervousness than does ephedrine.

Carbinoxamine maleate is an orally effective anti-histaminic agent that causes minimal side effects in man and animals. It is rapidly absorbed from the gastrointestinal tract, but its distribution and fate, like that of other anti-histaminics, is not yet known.

Ascorbic Acid (Vitamin C) plays an important part in the defence mechanisms of the body. Certain authorities reported that a possible relationship exists between the daily intake of ascorbic acid and resistance to infection.

*Indications:* Carbotuss Tablets provide anti-tussive, anti-histaminic, anti-pyretic, analgesic and decongestant effects of value in reducing the symptoms of the common cold.

*Advantages:*

* Carbotuss provides prompt symptomatic relief in common cold
* suppresses cough as effectively as codeine
* provides useful anti-histaminic action with minimal side effects
* strengthens defence mechanism of the body
* Carbotuss is non-narcotic
* there is no danger of addiction with Carbotuss
* side effects are negligible

*Dosage:* One or two Carbotuss Tablets should be taken at the first indication of a cold. Thereafter, one tablet four times daily.

*Supply:* Carbotuss Tablets are supplied in bottles of 20 and 100.

## CLORUBRA® Injection

Squibb Thiamine, Pyridoxine, Cyanocobalamin Injection

Clorubra is a combination of vitamins $B_1$, $B_6$ and $B_{12}$ for prevention and treatment of their deficiency states.

Each 2 ml. of Clorubra contains:

| | | |
|---|---|---|
| Thiamine Hydrochloride | 100 | mg. |
| Pyridoxine Hydrochloride | 50 | mg. |
| Cyanocobalamin | 1000 | mcg. |
| Benzyl alcohol (as preservative) 1.5% q.s. | 2 | ml. |

*Action :*

*Thiamine (Vitamin $B_1$)*:

Thiamine plays a vital role in metabolism as a prosthetic group for the enzymes involved in decarboxylation of important metabolic intermediates like pyruvic and alpha-ketoglutaric acids. Thiamine, therefore, serves an important function in intermediary metabolism. Deficiency of this vitamin leads to the condition known as beri-beri, The principal symptoms of thiamine deficiency are related to the nervous and the cardiovascular systems, and to some extent, the gastrointestinal tract. Administration of thiamine produces a dramatic response in individuals with beri-beri. alcoholic neuritis, peripheral neuritis of pregnancy and cardiovascular disease and gastrointestinal disorders of nutritional origin.

*Pyridoxine (Vitamin $B_6$)*:

Pyridoxine serves a vital role in metabolism as a coenzyme for a wide variety of metabolic transformations of aminoacids. Deficiency of pyridoxine produces changes in the skin, CNS and the erythropoietic system. Seborrhoea-like skin lesions about the eyes, nose and the mouth, glossitis and stomatitis can occur due to pyridoxine deficiency. Epilepsy and peripheral neuritis are the two manifestations of pyridoxine deficiency on the nervous system. Pyridoxine is often given prophylactically, and justifiably, to patients receiving isoniazid. A favourable response to pyridoxine therapy has been elicited when it is used to control the nausea and vomiting of pregnancy (hyperemesis gravidarum) and radiation sickness.

In patients with pyridoxine deficiency normoblastic anaemia is the rule. In a few cases, however, megaloblastic anaemia responding to pyridoxine makes this vitamin useful.

*Cyanocobalamin (Vitamin $B_{12}$)*:

The cobalamins appear to be involved directly or indirectly in every known metabolic system in man. They are essential for normal growth and nutrition, haemopoiesis, production of epithelial cells and the maintenance of myelin sheath

of the nervous system. Deficiency of cyanocobalamin results in the development of pernicious anaemia syndrome. Treatment with cyanocobalamin is aimed at replacement of depleted body stores and a constant maintenance of adequate supply. Cyanocobalamin is quantitatively and rapidly absorbed when injected intramuscularly or subcutaneously, peak levels being reached within an hour after the intramuscular injection. The need to inject cyanocobalamin is due to the relatively poor absorption of cyanocobalamin when given by the oral route. Thus the high blood levels produced by injection will be effective in replenishing the body stores of vitamin $B_{12}$ in a short duration.

For the treatment of pernicious anaemia, whether presenting as haematologic or neurologic manifestation or a combination of both, cyanocobalamin (Vitamin $B_{12}$) is recommended by way of injections. The need to inject cyanocobalamin occurs when there is an inadequate secretion of intrinsic factor from the stomach. This may occur not only in Addisonian pernicious anaemia, but also in conditions where gastric mucosa is destroyed such as ingestion of corrosives, linitis plastica and neoplasms involving gastric mucosa. Gastric atrophy, subtotal and total gastrectomy, small bowel fistulas, extensive resection of the small intestine and small intestine disruption, sprue, small bowel lymphoma and Whipple's disease (intestinal lipodystrophy) require parenteral supplementation of vitamin $B_{12}$. Infestation with fish tape worm (Diphyllobothrium latum), the 'blind loop' syndrome, megaloblastic anaemia sometimes seen with chronic liver disease and regional ileitis also produce vitamin $B_{12}$ deficiency necessitating parenteral supplementation.

Although nutritional macrocytic anaemia and megaloblastic anaemia of infancy and pregnancy require folic acid for their treatment, cyanocobalamin may also be indicated if vitamin $B_{12}$ deficiency is involved.

*Advantages:* Clorubra provides prompt vitamin supplementation, a wide range of clinical applications, rare hypersensitivity reaction, and a high concentration of vitamin $B_{12}$ It needs no reconstitution or special precautions for preservation.

*Indications:* Beri-beri, alcoholic neuritis, peripheral neuritis of pregnancy, cardiovascular disease of nutritional origin, gastrointestinal disorders of nutritional origin and neuralgias, such as trigeminial neuralgia and intercostal neuralgia.

Seborrhoeic dermatitis, epilepsy or peripheral neuritis due to pyridoxine deficiency; glossitis, stomatitis, hyperemesis gravidarum, radiation sickness and patients receiving isoniazid therapy.

In all types of megaloblastic anaemia due to chronic liver disease, infestation with Diphyllobothrium latum, small intestinal abnormalities, sprue, Whipple's disease, conditions leading to degeneration of gastric mucosa, such as linitis plastica, gastric atrophy, poisoning due to ingestion of corrosives, after gastrectomy, degenerative spinal disease, and herpes zoster.

*Contraindications:* This preparation is contraindicated in patients where parenteral administration of solutions containing thiamine has caused severe allergy or anaphylaxis.

*Side Effects and Precautions:* This preparation should be used with caution in persons

having a history of significant allergic reactions to thiamine. Sensitivity tests should be performed before administering a therapeutic dose. Whenever such reactions occur, the drug should be discontinued. Administration of adrenaline, corticosteroids and antihistamines may be given for controlling sensitivity reactions.

*Administration and Dosage:* Clorubra should be administered by deep intramuscular injection. In severe cases one injection is given daily until the acute symptoms disappear, followed by one ampoule 2-3 times a week; in milder conditions this dosage may be sufficient from the beginning. A maintenance dose of one ampoule once a week to once a month may be required continuously for patients requiring vitamin $B_{12}$.

*Supply:* Clorubra is available in ampoules, each containing 2 ml. of solution.

*Expiration date* 15 months. Store in a cool place.

## CRYSTICILLIN®

**Sterile Powder**

Squibb Procaine Penicillin G for Aqueous Injection

Crysticillin is available as a sterile powder in vials supplying 3,000,000 units (10 doses) of crystalline procaine penicillin G. The product is prepared for injection by adding 8.2 ml. aqueous diluent and vigorously shaking the vial to assure a uniform suspension.

*Indications:* Specific indications for Crysticillin and suggested dosage regimens are listed in the *Therapy Guide*. Penicillin therapy is effective only when the causative organism is penicillin-susceptible and the dosage is sufficient to produce bacteriostatic or bactericidal concentrations at the site of infection for a period long enough to allow body defences to eradicate the infection.

Prophylactic use of penicillin is recommended for prevention of possible secondary infections following tonsillectomy and tooth extraction in patients with rheumatic heart disease (or history of rheumatic fever), congenital heart disease or other conditions in which secondary infection may occur.

*Blood Levels:* Injections of 300,000 units Crysticillin produce a high initial blood level—in most patients a peak of 1 to 1.5 units penicillin/ml. serum occurs within 1 or 2 hours. Thereafter there is a gradual decline in the blood concentration although demonstrable levels are present in most patients at the end of 24 hours. The prolonged effect is shortened in ambulatory patients.

Blood level data are not conclusive evidence of the therapeutic efficacy of a given dosage regimen. The clinical response of the patient and the nature of the disease should determine dosage and frequency of administration.

*Administration:* Injection is made rapidly by the intramuscular route, following aspiration to be sure the needle is not in a vein. The preferred site is the upper outer quadrant of the buttock. Injections are easier to make and there is less likelihood of needle blockage if a small bore syringe is used; use a 20-gauge needle. Avoid using a syringe with a loosely fitting plunger as crystals may creep between the walls and cause it to "freeze". Remove the needle and plunger from the syringe soon after injection to prevent "freezing" of the remaining crystals.

*Dosage:*

## THERAPY GUIDE

| *Condition* | *Daily Dosage Intramuscularly* | *Duration of Treatment* | *COMMENTS* |
|---|---|---|---|
| Infections caused by *Staphylococcus* (susceptible strains) *Streptococcus Pneumococcus* | 300,000 to 600,000 u. | Continue until temperature is normal for 48 hr. and all manifestations of active infection disappear | In severe infections, higher dosage or soluble penicillin at frequent intervals may be required. In case of infections due to staphylococci, higher dosage may be required and sensitivity tests should be made to determine whether penicillin and/or other antibiotics should be employed. Indicated surgical procedures should be carried out in all cases. Streptococcal infections should be treated for 10 days in order to guard against the risk of rheumatic fever or glomerulonephritis. |
| Subacute Bacterial Endocarditis If causative organism is sensitive to 0.1 u. or less of penicillin per ml. | 600,000 u. or more q. 6 h. | Continue for a minimum period of 4 to 6 weeks. | Perform sensitivity tests before and periodically during treatment. Supplemental administration of streptomycin may be advisable. If sensitivity of organism exceeds 0.1 u. per ml. or if response is unsatisfactory, administer larger and more frequent doses of penicillin G potassium; when infection is under control, replace with large doses of aqueous procaine penicillin. |
| Gonorrhoea acute, uncomplicated | 1,200,000 u. to 2,400,000 u. for single injection or in two divided dosages in two buttocks consecutively at the same sitting | | In chronic and complicated cases intensify dosage and prolong treatment until cure is effected. Where concomitant syphilis is suspected, make darkfield examination before treatment and serologic tests monthly for 3 months. |
| Syphilis Primary and secondary; and latent with negative spinal fluid. | 600,000 u. | Continue for 10 days | |

| *Condition* | *Daily Dosage Intramuscularly* | *Duration of Treatment* | *COMMENTS* |
|---|---|---|---|
| Latent with no spinal fluid examination | 600,000 u. | Continue for 10 days | The possibility of asymptomatic neurosyphilis must be considered. |
| Late (including symptomatic and asymptomatic neurosyphylis, cardiovascular, osseous, cutaneous, and visceral) | 600,000 u. | Continue until a total of 6,000,000 to 9,000,000 u. has been given. | Any benefit from more than 10,000,000 units has not been demonstrated. |
| Early congenital (children under 2 years of age) | according to body weight | | A total of 100,000 u. per Kg. of body weight should be given in divided doses at 2 to 3 day intervals. |
| Late congenital | | | Treat as for corresponding stages of acquired syphilis. In children under 12, adjust dosage to age and weight. Interstitial keratitis usually does *not* respond to penicillin. The addition of corticosteroids applied locally to the eyes is recommended. |
| Syphilis in pregnancy | | | Treatment should correspond to the stage of the disease. |

The daily dosage for the following infections is: certain strains of Actinomycosis (with sulphonamides) 1 to 5 million units; Anthrax 600,000 to 1.2 million units; Clostridial infections (with antitoxin) minimum of 20 million units; Diphtheria (with antitoxin) up to 2 million units; Erysipeloid (swine erysipelas) up to 1.2 million units; Ratbite fever (caused by *Spirillum minus*) 1.2 million units; Relapsing fever 300,000 to 600,000 units; Vincent's infection 300,000 to 600,000 units. Treatment should generally continue for at least 48 hours after signs of infection have disappeared or temperature has returned to normal.

For prophylaxis in patients with rheumatic fever or rheumatic or congenital heart disease who are to undergo tonsillectomy, tooth extraction or other minor surgery, the recommended dosage is either 600,000 units of intramuscular procaine penicillin G daily or 500,000 units of oral potassium penicillin G four times daily for five days beginning two days before surgery and continuing for two days postoperatively. If oral penicillin is used, it should be supplemented by 600,000 units intramuscularly on the day of surgery.

*Precautions:* There are two active components in Crysticillin, penicillin and procaine, and it has not been shown that any specific toxicity is produced by their combination as procaine penicillin. Any reactions observed can be ascribed to one or the other component.

*Penicillin:* There is evidence that toxic reactions to procaine penicillin are somewhat less common than to penicillin alone. Toxic reactions due to penicillin have been largely limited to sensitivity phenomena. Such reactions may include urticaria, serum sickness-like reactions (fever, rash, arthralgia), other skin rashes,

and, rarely, anaphylactoid shock. They are more likely to occur in individuals with a history of allergy, asthma, hay fever, or urticaria, and in those who have previously demonstrated hypersensitivity to penicillin. Urticarial, serum sickness-like and other skin rash reactions may be controlled by anti-histamines and, if necessary, corticosteroids. Whenever such reactions occur, penicillin should be discontinued unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy. Serious anaphylactoid reactions are not controlled by anti-histamines, and require such measures as the immediate use of epinephrine, oxygen, and intravenous corticosteroids.

Evidence of the possible overgrowth of non-susceptible organisms should be looked for when any penicillin is administered.

*Procaine:* The most common toxic reaction to procaine—neurologic changes such as excitement, apprehension, twitching and convulsions—is caused by overdosage. But the small amount of procaine in Crysticillin makes the possibility of such reactions remote, except in procaine idiosyncrasy or hypersensitivity. Oxygen and intravenous barbiturates are indicated should such changes occur.

In rare cases procaine sensitivity may produce a circulatory reaction with pallor, tachycardia, chest pain, diplopia and blurring of vision, or sudden collapse characterized by circulatory failure. Administer artificial respiration and oxygen immediately; in this type of reaction intravenous barbiturates are ineffective.

Where procaine sensitivity is suspected, perform a preliminary intradermal skin test. If the test is positive, do not administer procaine penicillin.

*Supply:* Vials of 3,000,000 units (10 doses); Boxes of 5 vials.

*Expiration date* 30 months at room temperature in the dry state. Sterile suspensions may be kept for 1 week at room temperature and for 21 days if refrigerated. *Shake well before use.*

## CRYS-4®, CRYS-8® and CRYS-12® — Sterile Powder

Squibb Procaine Penicillin G Fortified with
Buffered Crystalline Sodium Penicillin G, for Aqueous Injection

CRYS-4 is the fortified aqueous procaine penicillin which comes in 3 strengths for the routine use in susceptible infections and for more severe infections, and highly resistant infections.

| | *Crystalline Sodium Penicillin G* | *Procaine Penicillin G* | *Required amount of diluent* | *Total volume of Injection* |
|---|---|---|---|---|
| CRYS-4 | 100,000 units | 300,000 units | 0.9 ml. | 1.1 ml. |
| CRYS-4 (5 dose) | 500,000 units | 1,500,000 units | 4.0 ml. | 5.1 ml. |
| CRYS-8 | 200,000 units | 600,000 units | 0.6 ml. | 1.1 ml. |
| CRYS-12 | 300,000 units | 900,000 units | 1.0 ml. | 1.9 ml. |

*Action:* With all three preparations the initial penicillin blood level is high, and a satisfactory level is maintained for protracted periods. The difference is in the

degree of height and duration, which are adopted to the treatment of infections that are more or less severe, and that have varying degrees of bacterial resistance.

*Indications:* Specific indications and suggested dosage regimens are given in *Therapy Guide*. CRYS-4 is recommended for the prophylaxis and treatment of infections susceptible to penicillin. Penicillin therapy is effective only when the causative organism is penicillin-susceptible and the dosage is sufficient to produce bacteriostatic or bactericidal concentrations at the site of infection for a period long enough to allow body defences to eradicate the infection.

Prophylactic use of penicillin is recommended for prevention of possible secondary infections following tonsillectomy and tooth extraction in patients with rheumatic heart disease (or history of rheumatic fever), congenital heart disease or other conditions in which secondary infection may occur.

*Blood Levels:* Injections of 1 ml. CRYS-4 (300,000 units procaine penicillin G and 100,000 units penicillin G sodium) produce in most patients a peak blood level of 2 units or more penicillin/ml. serum within 1 or 2 hours. Therefore, the preparation is particularly advantageous when high penicillin blood levels are needed promptly. After the initial peak there is a gradual decline in the blood concentration although demonstrable levels are present in most patients at the end of 24 hours. The prolonged effect is shortened in ambulatory patients.

Blood level data are not conclusive evidence of the therapeutic efficacy of a given dosage regimen. The clinical response of the patient and the nature of the disease should determine dosage and frequency of administration.

*Administration:* CRYS-4 is administered by deep intramuscular injection; the preferred site is the upper outer quadrant of the buttock.

*Dosage:* One daily dose of CRYS-4 is usually sufficient for prophylaxis or for the treatment of mild infection. Larger and/or more frequent doses should be employed in proportion to the severity of the infection. In such cases single injections of CRYS-8 or CRYS-12 may be given.

THERAPY GUIDE

| *Condition* | *Daily Dosage Intramuscularly* | *Duration of Treatment* | *COMMENTS* |
|---|---|---|---|
| Infections caused by *Staphylococcus* (susceptible strains) *Streptococcus Pneumococcus* | 400,000 u. | Continue until temperature is normal for 48 hr. and all manifestations of active infection disappear. | In severe infections higher dosage or soluble penicillin at frequent intervals may be required. In case of infections due to staphylococci, higher dosage may be required and sensitivity tests should be made to determine whether penicillin and/or other antibiotics should be employed. Indicated surgical procedures should be carried out in all cases. Streptococcal infections should be treated for 10 days in order to guard against the risk of rheumatic fever or glomerulonephritis. |

| *Condition* | *Daily Dosage Intramuscularly* | *Duration of Treatment* | *COMMENTS* |
|---|---|---|---|
| Subacute Bacterial Endocarditis<br>If causative organism is sensitive to 0.1 unit or less of penicillin per ml. | 800,000 u. or more q. 6 h. | Continue for a minimum period of 4 to 6 weeks | Perform sensitivity tests before and periodically during treatment. Supplemental administration of streptomycin may be advisable.<br>If sensitivity of organism exceeds 0.1 u. per ml. or if response is unsatisfactory, administer larger and more frequent doses of potassium penicillin G. When infection is under control, replace with large doses of aqueous procaine penicillin. |
| Gonorrhoea, acute, uncomplicated | 1,200,000 u. to 2,400,000 u. in a single dose or in two divided doses at the same sitting | | In chronic and complicated cases intensify dosage and prolong treatment until cure is effected. Where concomitant syphilis is suspected, make darkfield examination before treatment and serologic tests monthly for 3 months. |
| Syphilis<br>Primary and secondary; and latent with negative spinal fluid | 800,000 u. | Continue for 10 days. | |
| Latent with no spinal fluid examination | 800,000 u. | Continue for 10 days | The possibility of asymptomatic neurosyphilis must be considered. |
| Late (including symptomatic and asymptomatic neurosyphilis, cardiovascular, osseous, cutaneous, and visceral) | 800,000 u. | Continue until a total of 8,000,000 to 10,000,000 u. has been given. | Any benefit from more than 10,000,000 units has not been demonstrated. |
| Early congenital (children under 2 years of age) | according to body weight | | A total of 100,000 u. per Kg. of body wt. should be given in divided doses at 2 to 3 day intervals. |
| Late congenital | | | Treat as for corresponding stages of acquired syphilis. In children under 12, adjust dosage to age and weight. Interstitial keratitis usually does *not* respond to penicillin. The addition of corticosteroids, applied locally to the eyes, is recommended. |
| Syphilis in pregnancy | | | Treatment should correspond to the stage of the disease. |

The daily dosage for the following infections is: certain strains of Actinomycosis (with sulphonamides) 1 to 5 million units; Anthrax 800,000 to 1.2 million units; Clostridial infections (with antitoxin) minimum of 20 million units; Diphtheria (with antitoxin) up to 2 million units; Erysipeloid (swine erysipelas) up to 1.2 million units; Ratbite fever (caused by *Spirillum minus*) 1.2 million units; Relapsing fever 400,000 to 800,000 units; Vincent's infection 400,000 to 800,000 units. Treatment should generally continue for at least 48 hours after signs of infection have disappeared or temperature has returned to normal.

For prophylaxis in patients with rheumatic fever or rheumatic or congenital heart disease who are to undergo tonsillectomy, tooth extraction or other minor surgery, the recommended dosage is either 800,000 units of intramuscular penicillin daily or 500,000 units of oral potassium penicillin G four times daily for five days, beginning two days before surgery and continuing for two days postoperatively. If oral penicillin is used, it should be supplemented by 800,000 units intramuscularly on the day of surgery.

*Precautions:* There are two active components in CRYS-4, penicillin and procaine, and it has not been shown that any specific toxicity is produced by their combination as procaine penicillin. Any reactions observed can be ascribed to one or the other component.

*Penicillin:* Toxic reactions due to penicillin have been largely limited to sensitivity phenomena. Such reactions may include urticaria, serum sickness-like reactions (fever, rash, arthralgia), other skin rashes, and, rarely, anaphylactoid shock. They are more likely to occur in individuals with a history of allergy, asthma, hay fever, or urticaria, and in those who have previously demonstrated hypersensitivity to penicillin. Urticarial, serum sickness-like and other skin rash reactions may be controlled by antihistamines and, if necessary, corticosteroids. Whenever such reactions occur, penicillin should be discontinued unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy. Serious anaphylactoid reactions are not controlled by antihistamines, and require such measures as the immediate use of epinephrine, oxygen, and intravenous corticosteroids.

Evidence of the possible overgrowth of non-susceptible organisms should be looked for when any penicillin is administered.

*Procaine:* The most common toxic reaction to procaine—neurologic changes such as excitement, apprehension, twitching, and convulsions—is caused by overdosage. But the small amount of procaine in CRYS-4 makes the possibility of such reactions remote, except in procaine idiosyncrasy or hypersensitivity. Oxygen and intravenous barbiturates are indicated should such changes occur.

In rare cases procaine sensitivity may produce a circulatory reaction with pallor, tachycardia, chest pain, diplopia and blurring of vision or sudden collapse characterized by circulatory failure. Administer artificial respiration and oxygen immediately; in this type of reaction intravenous barbiturates are ineffective.

Where procaine sensitivity is suspected, perform a preliminary intradermal skin test. If the test is positive, do not administer procaine penicillin.

*Supply:*

| | |
|---|---|
| CRYS-4 | Vials of 400,000 units, boxes of 25 vials and 2,000,000 units (5 doses), boxes of 10 vials. |
| CRYS-8 | Vials of 800,000 units, boxes of 10 vials. |
| CRYS-12 | Vials of 1,200,000 units, boxes of 10 vials. |

*Expiration date* 24 months. May be stored at room temperature. Sterile suspension may be kept for 1 week without significant loss of potency if refrigerated.

## DI-ADEMIL®

**Tablets**

Squibb Hydroflumethiazide

Di-Ademil is a potent oral diuretic indicated in the control of oedema of varied aetiologies and in hypertension. Chemically, Di-Ademil (Squibb Hydroflumethiazide) is designated as 3, 4-dihydro-6-(trifluoromethyl)-1, 2, 4-benzothiadiazine-7-sulphonamide 1, 1-dioxide, and is related to chlorothiazide. It is one of a series of diuretics containing a trifluoromethyl group, a modification which appears to result in outstanding diuretic and antihypertensive action of extended duration, with minimal adverse effects on plasma electrolyte levels.

*Action:* Pharmacologic and clinical studies have demonstrated that Di-Ademil is one of the most potent oral diuretics currently available. Clinical comparison studies have shown that it produces an equivalent diuresis with about one-tenth the dosage required for chlorothiazide. When given in a dose one-tenth that of chlorothiazide, Di-Ademil exhibits the same antihypertensive properties but produces somewhat greater water and sodium output, with less potassium and bicarbonate loss. Di-Ademil therapy is outstandingly effective not only in establishing, but in maintaining excretion of retained fluid in oedematous patients. Moreover, the duration of action of hydroflumethiazide is sufficiently prolonged to allow a single daily administration in most patients.

Di-Ademil has both diuretic and antihypertensive action. It does not cause hypotension in normotensive individuals. Used alone or in conjunction with other antihypertensive agents, Di-Ademil permits great flexibility in the management of hypertension. When Di-Ademil is given alone to patients with mild hypertension, it may induce a significant lowering of the blood pressure within a week, and frequently to within the normal range by the end of the third week of therapy. When added to an established antihypertensive drug regimen Di-Ademil may produce a further lowering of blood pressure.

Di-Ademil is especially useful when long-term therapy is required, since the beneficial effects of Di-Ademil do not diminish with continuous daily administration. The optimal saluretic action of Di-Ademil obviates the need for drastic restriction of salt intake, and patients may enjoy a more palatable diet. The onset of diuretic action of Di-Ademil is rapid (within 3 hours), nevertheless the action is gentle and sustained (evenly distributed over 8 to 12 hours).

*Indications:* Di-Ademil is indicated in the management of oedema and whenever diuresis is required. Specifically, this potent diuretic is useful in the treatment of oedema in congestive heart failure, oedema of the pre-menstrual syndrome, oedema and toxaemia of pregnancy, oedema of nephrosis and nephritis, oedema of cirrhosis with ascites, and oedema induced by the use of drugs such as certain steroids. Clinical experience has shown that patients with allergic responses to chlorothiazide or those who have developed tolerance to the drug can be successfully transferred to Di-Ademil.

Di-Ademil also finds application in the management of hypertension alone or in conjunction with Raudixin® (Squibb Rauwolfia Whole Root) and other antihypertensive drugs such as the ganglionic blocking agents.

*Dosage:* The dosage should be individualized and adapted to the condition.

*Oedema:* To initiate therapy the suggested daily dose of Di-Ademil is 100 mg. given in divided doses, preferably morning and early afternoon, maintenance dosage may vary from 25 mg. to 100 mg. daily in divided doses morning and afternoon.

*Hypertension:* The suggested initial dose of Di-Ademil is 50 to 100 mg. daily, given in divided doses. The maintenance dosage may range from 25 to 50 mg. once or twice a day depending on response of the patient.

*Precautions:* No serious side effects attributable to Di-Ademil have been reported in clinical experience to date. A few cases of mild pruritus and minor gastro-intestinal disturbances have been reported. As with the use of any potent diuretic of this type, hypochloraemic alkalosis with or without hypokalaemia may occur in some individuals. Generally, a high dietary intake of potassium as afforded by citrus fruit juices as well as a balance diet of meat and vegetables helps to preclude the occurrence of these unwanted effects. Cirrhotic patients have been reported to show a particular proneness to the development of hypokalaemia. For this reason, cirrhotic patients or those whose sodium intake is rigidly restricted should be observed closely and at regular intervals for early signs of fluid and/or electrolyte disturbances so that appropriate corrective measures can be taken promptly.

Care should be exercised in administering a potent diuretic agent to patients with severely damaged kidneys or to those with renal insufficiency and increasing azotaemia. In the presence of complete renal shutdown, therapy with any diuretic agent (including Di-Ademil) is contraindicated.

Therapy with benzothiadiazine derivatives may result in increased glycaemia or glycosuria in diabetic patients and may unmask a diabetic predisposition in apparently normal individuals.

Increased serum uric acid concentrations have occurred occasionally; and a few instances of leg or abdominal cramps, and a few cases of pruritus, rash or other dermatologic manifestations have also been reported. Gastrointestinal disturbances (nausea, vomiting or gastric pain) may be encountered in some patients. As with any new drug entity, such complications as neutropenia, or purpura with or without thrombocytopenia and unusual manifestations suggestive of unusual sensitivity should be kept in mind.

*Supply:* Bottles of 20 and 100 tablets, each containing 25 mg. of hydroflumethiazide. May be stored at room temperature.

**DICRYSTICIN-S®** **Sterile Powder**

**DICRYSTICIN-S® "800"** **Sterile Powder**

**DICRYSTICIN-S® FORTIS** **Sterile Powder**

Squibb Streptomycin with Sodium and Procaine Penicillin G

Dicrysticin-S is supplied as a dry powder in 1 dose vials. Each dose of Dicrysticin-S provides 300,000 units procaine penicillin G, 100,000 units buffered crystalline

sodium penicillin G, and 0.5 Gm. pure streptomycin base in the form of streptomycin sulphate. The preparation also contains sodium citrate as a buffer.

Dicrysticin-S "800" is supplied as a dry powder in 1 dose vials. Each dose of Dicrysticin-S "800" provides 600,000 units procaine penicillin G, 200,000 units buffered crystalline sodium penicillin G and 0.5 Gm. of pure streptomycin base in the form of streptomycin sulphate. The preparation also contains sodium citrate as a buffer.

Dicrysticin-S Fortis is supplied as a dry powder in 1 dose vials. Each dose of Dicrysticin-S Fortis provides 300,000 units procaine penicillin G, 100,000 units sodium penicillin G, and 1.0 Gm. pure streptomycin base in the form of streptomycin sulphate. The preparation also contains sodium citrate as a buffer.

*Advantages:*

* of particular value in treating some mixed infections
* may be given in surgery where there is danger of contamination, particularly from the contents of a hollow viscous

*Indications:* Dicrysticin-S, Dicrysticin-S "800" and Dicrysticin-S Fortis are recommended in the treatment of peritonitis, mediastinitis, suspected brain abscess and other infections in which the causative organisms cannot be identified without unwarranted operative procedures. Whenever possible, however, a thorough search for the primary focus should be made in order to determine if sensitivity to these combinations warrants their use. They are also recommended in some mixed infections, particularly those involving both gram-positive and gram-negative organisms, e.g., those common in the respiratory or urogenital tract and in contaminated wounds. Dicrysticin-S, Dicrysticin-S "800" and Dicrysticin-S Fortis may be given in surgery where there is danger of contamination, particularly from the contents of a hollow viscous. When treatment is prolonged, as for subacute bacterial endocarditis, it is wise to perform periodic *in vitro* sensitivity tests to determine any change in the sensitivity of the causative organism.

*Note: Combination products with streptomycin and penicillin in the proportions provided by these preparations are not devised to meet paediatric needs. If the physician deems the concomitant administration of penicillin and streptomycin advisable in infants and children, dosage must be determined by the streptomycin content because of toxicity. (For details, see Dicrysticin-S Pediatric.)*

*Dosage:* The dose of Dicrysticin-S, Dicrysticin-S "800" or Dicrysticin-S Fortis should be determined primarily by the current recommended dosage of streptomycin. In surgical prophylaxis 1 dose of Dicrysticin-S or Dicrysticin-S "800" is injected every 8 or 12 hours beginning 1 or 2 days before surgery and continuing for 7 to 10 days postoperatively. The recommended dosage of Dicrysticin-S Fortis is 1 dose every 12 or 24 hours beginning 1 or 2 days before surgery and continuing for 7 to 10 days post-operatively. When larger amounts of Dicrysticin-S, Dicrysticin-S "800" or Dicrysticin-S Fortis are required, as in septicaemia or peritonitis, the total daily dosage should provide no more than 2 Gm. of streptomycin in the treatment of such infections as peritonitis, supplementary penicillin therapy may be advisable.

Probably the best guide to the duration of treatment is provided by the clinical

response of the patient. It is recommended that treatment be continued for 3 or 4 days after the temperature has returned to normal or cultures have become consistently negative.

*Administration:* 1. Suspend these preparations in sterile distilled water or sterile isotonic solution, in the following manner:

Dicrysticin-S: To provide a volume of 2 ml. per dose, add 1.5 ml. diluent to the 1 dose vial and 7.0 ml. to the 5 dose vial.

Dicrysticin-S "800": To provide a volume of 2 ml. per dose, add 1.6 ml. diluent to the 1 dose vial.

Dicrysticin-S Fortis: To provide a volume of 3 ml. per dose, add 2.5 ml. diluent to the 1 dose vial.

Direct the stream of diluent against the bottom of the vial.

Shake vigorously until all the diluent has been added and the suspension is smooth and uniform.

2. Inject air into the vial for easier withdrawal.

3. Have the suspension at room temperature before administration.

4. After withdrawing the dose into the syringe, make sure that the needle is empty by pulling the plunger back until a small air bubble appears.

5. Inject the suspension *intramuscularly*. The likelihood of painful injection is reduced if the following precautions are observed: Inject high in the upper outer quadrant of the buttock. Change the site for each injection. Insert needle deeply to avoid subcutaneous deposition. Inject slowly.

*Dicrysticin-S, Dicrysticin-S "800" and Dicrysticin-S Fortis should never be given intravenously.*

Avoid a loosely fitting plunger in the syringe. Procaine penicillin crystals may creep between the walls and cause it to "freeze". Remove the needle and plunger from the syringe soon after the injection to prevent "freezing" of remaining crystals. Wash before resterilization.

*Precautions:* There are three active components in these formulations: procaine, penicillin and streptomycin. It has not been shown that any specific toxicity results from the chemical combination of procaine with penicillin or the simultaneous administration of streptomycin. However, any unusual reactions should receive immediate medical attention.

*Penicillin:* Toxic reactions to penicillin are largely limited to hypersensitivity phenomena. The manifestations of hypersensitivity range from a mild erythema or urticaria to severe serum-sickness and rarely, anaphylactoid shock. Before these preparations are administered, the patient should be questioned as to previous evidence of sensitivity to penicillin or a history of bronchial asthma or allergy, all of which increase the likelihood of hypersensitivity. If a hypersensitivity reaction occurs that is more serious than the condition being treated, and it cannot be controlled, this medication should be discontinued. For the rare occurrence of anaphylactoid shock the physician should be prepared to institute

remedial measures immediately such as the administration of oxygen, vasopressor agents, and intravenous steroids.

*Procaine:* The most common toxic reactions to procaine—neurologic changes such as excitement, apprehension, twitching, and convulsions are caused by overdosage. The small amount of procaine in these preparations makes the possibility of such reactions remote. Oxygen and intravenous barbiturates are indicated should such neurologic changes occur.

In rare cases procaine sensitivity may produce a circulatory reaction with pallor, tachycardia, chest pain, diplopia and blurring of vision, or sudden collapse characterised by circulatory failure. Administer artificial respiration and oxygen immediately; in this type of reaction intravenous barbiturates are ineffective.

Where procaine sensitivity is suspected, perform a preliminary intradermal test. If the test is positive, do not administer Dicrysticin-S or Dicrysticin-S "800" or Dicrysticin-S Fortis.

*Streptomycin:* Streptomycin in sufficiently large doses may produce vestibular or auditory damage, of which vertigo and tinnitus are the most common symptoms. Such toxicity most often occurs after prolonged dosage. Streptomycin is less apt to produce auditory damage than is dihydrostreptomycin in comparable dosage. However, streptomycin is more apt to produce vestibular damage. Auditory impairment is usually permanent; vestibular damage may be permanent, but symptoms tend to disappear as the patient adjusts and learns to compensate visually. Ability to compensate for vestibular impairment decreases with age. Streptomycin preparations, therefore, should be used with caution in elderly patients.

The caloric stimulation test for vestibular function and audiometric tests are advisable during prolonged streptomycin therapy to detect signs of developing eighth nerve damage; tests should be made before treatment is started and periodically thereafter.

The blood concentration of streptomycin should not exceed 20 to 25 micrograms/ml. plasma. Pre-existing renal impairment interferes with streptomycin excretion, producing high blood levels and increasing the risk of vestibular and auditory dysfunction.

Skin or allergic reactions occur infrequently and can usually be controlled with antihistaminic agents.

Signs of kidney involvement (proteinuria, haematuria and occasional azotaemia) generally disappear on withdrawal of the drug. Unless renal function is impaired, changes in the urine are usually not cause for interrupting therapy.

Headache, paraesthesias of the face, and gastric disturbances may occur. Clinical judgment as to termination of therapy must be exercised when such side effects occur.

Evidence for the possible overgrowth of non-susceptible organisms must be looked for when antibiotics are administered.

*Supply:* Dicrysticin-S, 1 dose, boxes of 25 vials; and 5 dose, boxes of 10 vials. Dicrysticin-S "800" and Dicrysticin-S Fortis, 1 dose, boxes of 10 vials.

*Expiration date* for all these preparations, 24 months at room temperature. Sterile suspensions may be kept in the refrigerator for 1 week without significant loss of potency.

## DICRYSTICIN-S® PEDIATRIC — Sterile Powder

Squibb Streptomycin with Sodium and Procaine Penicillin G

Dicrysticin-S Pediatric is supplied as a dry powder in one dose vials. Each dose of Dicrysticin-S Pediatric provides 300,000 units procaine penicillin G, 100,000 units buffered crystalline sodium penicillin G and 0.25 Gm. of pure streptomycin base in the form of streptomycin sulphate.

Dicrysticin-S Pediatric is indicated for prophylaxis before and after surgery in or near a contaminated site; for the treatment of certain mixed infections caused by both gram-positive and gram-negative organisms, particularly chronic infections of the respiratory or urogenital tract; for the treatment of infections in which the causative organism cannot be readily identified, especially peritonitis, mediastinitis or brain abscess (in such cases, however, whenever possible, a thorough search for the primary focus should be made in order to determine if sensitivity to this antibiotic combination warrants its use); and for the treatment of selected cases of septicaemia or subacute bacterial endocarditis in which there is *in vitro* evidence that the combination of penicillin and streptomycin has an additive or synergistic effect. When treatment is prolonged, as for subacute bacterial endocarditis, it is wise to perform periodic sensitivity tests to determine any change in the sensitivity of the causative organism. Dicrysticin-S Pediatric may be effective in infections where the bacteria are relatively more resistant to penicillin or streptomycin drugs alone than to the combination.

*Dosage:* The dose of Dicrysticin-S Pediatric should be determined primarily by the currently recommended dosage of streptomycin. The best guide to the duration of treatment is provided by the clinical response of the patient. The following schedule is recommended:

| | *Daily Dose |
|---|---|
| Under 1 year | 0.8 ml. (½ vial) |
| Under 3 years | 1.65 ml. (1 vial) |
| Under 6 years | 1.65 to 3.3 ml. (1 to 2 vials) |
| More than 6 years | 3.3 ml. (2 vials) |

*Administration:* One of the outstanding features of Dicrysticin-S Pediatric is ease of administration. For reconstitution, Dicrysticin-S Pediatric may be suspended in sterile distilled water or sterile isotonic sodium chloride. To provide a volume approximately of 1.65 ml. per dose of Dicrysticin-S Pediatric add 1.2 ml. diluent to the vial. The administration is a matter of simple *intramuscular* injection after aspirating to be sure that the needle is not in a vein.

*Note: This product should never be given intravenously.*

* Either as a single dose or 2 equally divided doses per day. In more severe infections the dosage may be doubled.

Dicrysticin-S Pediatric in powder form is stable at room temperature. Sterile suspension may be kept in the refrigerator for 1 week without significant loss of potency.

*Supply:* Vials of 1 dose (1.2 ml. diluent to be added), boxes of 25 vials.

*Expiration date* 24 months. May be stored at room temperature.

## DI-RAUDIXIN® Tablets

## DI-RAUDIXIN® FORTE Tablets

Squibb Standardized Whole Root
Rauwolfia Serpentina (Raudixin®)
and Hydroflumethiazide (Di-Ademil®)

Di-Raudixin conveniently combines the anti-hypertensive tranquillizer Raudixin (Squibb Standardized Whole Root Rauwolfia Serpentina) and the anti-hypertensive diuretic Di-Ademil (Squibb Hydroflumethiazide) in a single tablet. The resulting anti-hypertensive effect is potentiated, being greater than that obtained with either component alone. As a result, Di-Raudixin provides effective therapy for all degrees of hypertension. It lowers blood pressure safely and dependably—there are no extremes or sudden drops in pressure when the patient is on Di-Raudixin. Di-Raudixin is available in two potencies: Di-Raudixin—50 mg. Raudixin and 25 mg. Di-Ademil and Di-Raudixin Forte—50 mg. Raudixin, and 50 mg. Di-Ademil.

*Action:* The action of Di-Raudixin is essentially due to its two components, i.e., Raudixin and Di-Ademil.

Whole root *Rauwolfia Serpentina* (Raudixin), one of the two basic components of Di-Raudixin, is a time-tested anti-hypertensive agent whose value has been confirmed by the evidence of many years of growing clinical use. Raudixin, being *standardized* whole root, has a greater and more balanced therapeutic action than can be produced by any single Rauwolfia alkaloid. It has three basic pharmacologic effects: it lowers systolic and diastolic blood pressure, provides tranquillization, and induces a mild reduction in pulse rate. Reduction in blood pressure is both gradual and sustained, thus protecting the patient against sharp fluctuations. Normotensive individuals are not significantly affected. Raudixin's mild sedative action tends to depress the aggravating effects of emotional tension and upsets. This tranquillizing effect is also valuable in helping to alleviate other common hypertensive symptoms such as irritability, headache, anxiety, insomnia, and palpitations. Patients generally experience a feeling of well-being, emotional difficulties occur less frequently, there is less likelihood of depression. The mild bradycardia lowers the work load of the heart, helping to increase cardiac efficiency. Raudixin potentiates other anti-hypertensive agents—when used in combination lesser amounts of the more potent and toxic drugs can be used.

Raudixin is clinically reliable and effective on continued administration. It causes no liver dysfunction. Tolerance and cumulation have not been reported.

The Di-Ademil component is a benzothiadiazine derivative, a potent antihypertensive diuretic. Its structural formula is 3, 4-dihydro-6-(trifluoromethyl)-1, 2, 4-

benzothiadiazine-7-sulphonamide-1, 1-dioxide. Clinical studies have shown that 100 mg. Di-Ademil have therapeutic effect equivalent to 1000 mg. of the chemically related chlorothiazide. Potassium excretion is notably less with Di-Ademil. Di-Ademil lowers blood pressure smoothly and significantly and is useful in all degrees of hypertension, whether alone or in combination with other potent antihypertensive agents.

The antihypertensive actions of Raudixin and Di-Ademil are complementary and the combination of both in Di-Raudixin and Di-Raudixin Forte elicit more favourable therapeutic response than could be expected with either one of its components.

These preparations complement the hypotensive action of ganglionic blocking agents or hydralazine, permitting and even necessitating considerably smaller doses of these more toxic drugs and thereby decreasing the incidence and severity of their side effects.

*Advantages:* Di-Raudixin and Di-Raudixin Forte provide numerous and significant beneficial effects in the management of *all degrees* of hypertension.

Di-Raudixin and Di-Raudixin Forte offer—

*all the advantages of Raudixin*

* standardized whole root Rauwolfia serpentina
* gentle, gradual antihypertensive action—the "Rauwolfia preparation of choice"
* tranquillization to help relieve common emotional aspects of hypertension such as anxiety, tension, headache, insomnia, and palpitations
* mild bradycardia to lower the work load of the heart and help increase cardiac efficiency
* non-habituation
* fewer gastrointestinal side effects
* long-term safety (has been given continuously for years)

*plus*

*all the advantages of hydroflumethiazide*

* unsurpassed diuretic action for prompt attainment of an oedema-free state
* effective sustained antihypertensive action
* virtual absence of drug tolerance
* minimal effects on electrolyte balance and blood chemistry
* reduced need for salt restriction
* low incidence of side effects

*plus*

* increased efficacy sufficient for all degrees of essential hypertension
* complementary antihypertensive action permitting smaller doses of both components
* complementary antihypertensive effect permitting and necessitating reduced dosage, by as much as one-half of other antihypertensive drugs such as ganglionic blocking agents or hydralazine
* gentle, gradual, sustained reduction of systolic and diastolic blood pressure, more efficient control of hypertension on a convenient, simplified dosage schedule

* particularly effective in hypertensive cardiovascular conditions manifesting oedema
* well-tolerated over extended periods of administration
* no contraindications, except in the presence of complete renal shutdown

*Indications:* Di-Raudixin and Di-Raudixin Forte are effective in all degrees of hypertension. Their gentle, safe, wide-range antihypertensive action is particularly useful when blood pressure reduction is required; when there are signs of congestive failure or oedema; when there is insufficient response to a single antihypertensive agent; when partial or complete replacement of potentially more toxic antihypertensive drugs is desirable.

Di-Raudixin and Di-Raudixin Forte are sufficient for most hypertensive patients. When an additional antihypertensive effect is needed, however, more drastic antihypertensive agents may be used concomitantly. Both afford smoother control of blood pressure and permit and even necessitate considerable lower dosage of these more toxic hypotensive agents. After an adequate response is obtained and maintenance dosages established, it may gradually be possible to eliminate the other agents and maintain the patient on Di-Raudixin or Di-Raudixin Forte.

Both Di-Raudixin and Di-Raudixin Forte are indicated for all degrees of hypertension. Di-Raudixin, however, may be of greatest value for long-term maintenance therapy of hypertension, when associated oedema has been satisfactorily relieved or a higher ratio of the Raudixin component to the Di-Ademil component is needed.

*Dosage:* Dosage should be adjusted to individual requirements.

DOSAGE SUMMARY

| *Dosage Strength* | *Indication* | *Daily Regimen* |
|---|---|---|
| Di-Raudixin<br>50 mg. Raudixin<br>25 mg. Di-Ademil | All degrees of hypertension but where a lower dose of the diuretic is desired | 1 to 3 tablets daily depending on patient response. |
| Di-Raudixin Forte<br>50 mg. Raudixin<br>50 mg. Di-Ademil | All degrees of hypertension, especially when the patient is markedly oedematous | Initial dosage range 1 to 3 tablets, preferably in divided doses, morning and afternoon.<br><br>Maintenance—as low as 1 tablet daily may suffice. |

When either Di-Raudixin or Di-Raudixin Forte is used concomitantly with ganglionic blocking agents, the dosage of these latter drugs should be reduced by one-half.

*Precautions:* Raudixin is remarkably well tolerated over extended periods of administration. Since the combined use of Raudixin and Di-Ademil makes possible lower doses of rauwolfia, the likelihood of any unwanted effects is diminished. Rauwolfia side effects such as diarrhoea, weight gain, nausea and vomiting, drowsiness, nasal congestion, increased dreaming and reversible extrapyramidal symptoms are less likely to occur with the Di-Raudixin regimen.

No serious side effects attributable to Di-Ademil have been reported in clinical

trials to date. A few cases of mild pruritus and minor gastrointestinal disturbances have been reported. As with any potent diuretic of this type, however, a rare hypochloraemic alkalosis with or without hypokalaemia may occur. Generally, a high potassium intake as supplied by orange or tomato juice and a balanced diet of meat and vegetables helps preclude these unwanted effects.

Patients with hepatic cirrhosis are particularly prone to hypokalaemia. Therefore cirrhotic patients should be observed closely and regularly to detect early signs of fluid and/or electrolyte disturbance so that appropriate corrective measures can be taken promptly. Care should be taken in treating patients with severely damaged kidneys and low urine output.

*Note:* There are no absolute contraindications to the use of Di-Raudixin except complete renal shutdown. However, any preparation containing rauwolfia should be used with caution in patients with a history of depression, peptic ulcer or ulcerative colitis.

*Supply:* Di-Raudixin (both potencies) is supplied as capsule-shaped tablets in bottles of 20 and 100.

## ENGRAN® — Tablets

Squibb Vitamin-Mineral Supplement

Whenever vitamin-mineral supplementation is required, just 1 Engran Tablet daily provides high supplemental dosages of the essential vitamins to help meet increased nutritional requirements. In each small tablet, Engran supplies high supplemental dosages of the essential vitamins, supplemental calcium in phosphorus-free form, supplemental iron, plus trace elements.

Each Engran Tablet supplies:

VITAMINS

| | |
|---|---|
| Vitamin A | 5,000 I.U. |
| Vitamin D | 500 I.U. |
| Vitamin $B_1$ | 3 mg. |
| Vitamin $B_2$ | 3 mg. |
| Vitamin $B_6$ | 2 mg. |
| Vitamin $B_{12}$ | 2 mcg. |
| Folic Acid | 1 mg. |
| Niacinamide | 20 mg. |
| Calcium Pantothenate | 5 mg. |
| Vitamin C | 75 mg. |
| Vitamin K | 0.5 mg. |

MINERALS

| | |
|---|---|
| Calcium | 0.15 Gm. |
| Iodine | 0.15 mg. |
| Iron | 10 mg. |
| Potassium | 5 mg. |
| Copper | 1 mg. |

| | |
|---|---|
| Manganese | 1 mg. |
| Magnesium | 6 mg. |
| Zinc | 1.5 mg. |

*Indications:* Engran is indicated as a dietary supplement during pregnancy, lactation, or whenever routine vitamin-mineral supplementation is required.

*Dosage:* 1 Engran Tablet daily, or as indicated.

*Supply:* Capsule-shaped tablets in bottles of 25 and 100.

*Note:* Keep tightly closed in a cool and dark place.

*Expiration date* 18 months.

## FUNGIZONE®

**Tablets**

Squibb Amphotericin B

Fungizone, Squibb Amphotericin B, is a polyene antibiotic produced by a strain of *Streptomyces nodosus*. The isolation and characterization of crystalline amphotericin B were achieved at The Squibb Institute for Medical Research. Each Fungizone Tablet contains 100 mg. amphotericin B.

*Action:* Fungizone inhibits the growth of a wide variety of yeasts and yeast-like fungi. The drug is well tolerated as an oral antifungal agent, and its efficacy is dependable for the prophylaxis or treatment of intestinal candidiasis. In humans, as in experimental animals, oral administration of amphotericin B in high doses produced at most only low blood levels (0.05 mcg./ml.) due to poor absorption of the drug from the gastrointestinal tract. Most of the orally administered drug is eliminated via the faeces.

*Indications:* Fungizone Tablets are indicated for the prophylaxis or treatment of intestinal candidiasis, including that sometimes induced by the broad spectrum antibiotics, and for the suppression of any intestinal reservoir of *Candida albicans* which may complicate cutaneous, mucocutaneous or vaginal candidiasis. For the latter purpose, Fungizone Tablets should be employed as an adjunct to other specific topical therapeutic measures.

*Dosage and Administration:* The suggested dosage for both adult and paediatric patient is (a) prophylactic: 50 or 100 mg., q.i.d., (b) therapeutic: 100 mg. q.i.d. However, if desired, substantially higher dosage may be employed without serious side effects or significant toxicity. The tablets may be administered to infants and young children by pulverizing, combining with water or milk, and utilizing a dropper.

*Toxicity:* Probably because of its very limited absorption, Fungizone Tablets are virtually nontoxic and non-sensitizing and are well tolerated by all age groups including debilitated infants, even on prolonged administration.

*Supply:* Bottles of 12 tablets.

*Expiration date* 12 months.

## FUNGIZONE®-S OTIC DROPS — Liquid

Squibb Amphotericin B with Neomycin-Gramicidin (Spectrocin®)

Fungizone-S Otic Drops is Squibb Amphotericin B with Spectrocin (Neomycin and Gramicidin) in propylene glycol.

Each ml. of Fungizone-S Otic Drops contains:

| | |
|---|---|
| Neomycin base | 3.5 mg. |
| Gramicidin | 1.0 mg. |
| Amphotericin B | 30.0 mg. |
| Benzocaine | 14.0 mg. |

Propylene glycol: Glycerin (3:1) base q.s. ..... .1 ml.

*Action and Uses:* Fungizone-S Otic Drops has bactericidal and fungicidal action. It provides a combination of antibacterial and antifungal antibiotics effective against a wide variety of gram positive and gram negative organisms including fungi commonly encountered in otic infections.

Fungizone-S Otic Drops is indicated for the treatment of infections, pain and itching associated with otitis externa, otitis media with a perforated tympanic membrane, post-operative aural cavities and furunculosis of the ear.

*Contraindications:* This product is contraindicated in individuals with a history of hypersensitivity to any of its components.

*Precautions:* The possibility of neomycin ototoxicity due to prolonged use should be borne in mind when this drug is used in cases of chronic suppurative otitis media. As with all antibiotics, prolonged use may result in overgrowth of non-susceptible organisms. If superinfection occurs, appropriate measures should be instituted.

*Administration:* After preliminary cleaning, three to four drops are instilled in the infected ear two to three times daily. The drops should be instilled with the affected ear turned upwards and the position maintained for a minute to facilitate penetration.

Care should be taken to shake the bottle well before use.

*Supply:* Bottles of 5 ml. with dropper.

*Expiration date* 12 months.

## KENACOMB®

**Ointment**

Squibb Triamcinolone Acetonide, Neomycin-Gramicidin (Spectrocin®) and Nystatin (Mycostatin®)

Kenacomb is a highly effective dermatologic preparation that has four basic therapeutic effects: anti-inflammatory, antipruritic, antibacterial and antifungal. It is especially formulated for skin conditions caused or complicated by bacterial and/or monilial infection and for which potent, dependable anti-inflammatory, antipruritic action is also desired. Kenacomb combines the anti-inflammatory corticoid, Triamcinolone Acetonide, the wide-spectrum antibacterial, Spectrocin (Squibb Neomycin-Gramicidin) and the antifungal antibiotic Mycostatin (Squibb Nystatin) in Plastobase® (Squibb Plasticized Hydrocarbon Gel).

Each gramme of Kenacomb supplies:

| | |
|---|---|
| Triamcinolone Acetonide | 1.0 mg. (0.1%) |
| Neomycin Base (as sulphate) | 2.5 mg. |
| Gramicidin | 0.25 mg. |
| Nystatin | 100,000 units |

Kenacomb reduces inflammation, relieves itching and combats or prevents bacterial and monilial infections.

* TRIAMCINOLONE ACETONIDE is an outstanding topical corticosteroid. Proved clinically superior wherever topical corticoids are indicated, triamcinolone acetonide is distinguished by its marked anti-inflammatory, antipruritic, antiallergic effects. It provides rapid, complete, often prolonged relief of itching, burning and cutaneous inflammation.

Paired comparison studies with 1.0% hydrocortisone and 0.5% prednisolone preparations have shown that triamcinolone acetonide in 0.1% concentration, usually acts faster and produces more complete therapeutic results. Moreover, triamcinolone acetonide is frequently effective in those instances where hydrocortisone and other corticosteroids fail to bring about a good or complete therapeutic response.

* SPECTROCIN combines the broad spectrum activities of two potent topical antibiotics, neomycin and gramicidin. The joint actions of these powerful anti-infectives provide comprehensive antibacterial therapy against a wide range of gram-positive and gram-negative bacteria, including those responsible for most bacterial skin infections.

* MYCOSTATIN is the antibiotic of choice for treating or preventing cutaneous *Candida* (monilia) *albicans* infections. The first safe antifungal antibiotic, Mycostatin is uniformly effective in most local monilial infections.

Plastobase® (Squibb Plasticized Hydrocarbon Gel), the vehicle in Kenacomb Ointment, is a combination of 95% Liquid Petrolatum and 5% polyethylene, an inert plastic. Liquid Petrolatum is thickened and retained in gel form by a matrix

of solid polyethylene. As used in Kenacomb Ointment, Plastobase provides fast, regular and thorough release of medicaments and uniform dispersion of medicaments even at elevated temperatures. Consistently soft, Kenacomb Ointment is easily applied to the skin and is non-"running" at body temperature. It imparts a velvety, non-greasy feel to the skin and can be readily removed.

*Advantages:*

* four basic therapeutic effects in one preparation—anti-inflammatory, antipruritic, antibacterial, antifungal
* dramatically effective—provides rapid, complete, often prolonged relief of itching, burning, and inflammation, frequently when other topical steroids have failed
* a potent anti-infective—combats or prevents bacterial and/or monilial infections
* unusually well tolerated
* excellent patient acceptance

*Indications:*

* superficial bacterial infections
* cutaneous moniliasis
* lichen simplex chronicus
* anogenital pruritus (pruritus ani et vulvae)
* infantile eczema

The following conditions when threatened or complicated by bacterial and/or monilial superinfection:

* atopic dermatitis
* eczematoid dermatitis
* stasis dermatitis
* nummular dermatitis
* contact dermatitis
* exudative dermatitis
* seborrhoeic dermatitis
* neurodermatitis
* dermatitis venenata

*Administration:* Apply a thin film to the affected area 2 to 3 times daily.

*Contraindications:* Kenacomb is contraindicated in tuberculous and most viral lesions of the skin, herpes simplex, vaccinia and varicella particularly. It is also contraindicated in fungal lesions of the skin except candidiasis, and in patients with a history of hypersensitivity to any of its components.

*Precautions:* Kenacomb has been extremely well tolerated locally. Systemic toxicity has not been observed with topical applications of triamcinolone acetonide or any of the other active components. Sensitivity reactions to topically applied nystatin, triamcinolone acetonide, neomycin or gramicidin are only rarely encountered. With prolonged use of steroids in intertriginous areas or under occlusive dressings, striae may occur. Systemic side effects are a possibility when topical steroid preparations are used over large areas or over prolonged periods.

*Supply:* Tubes of 2.5 Gms. and 5 Gms.

*Expiration date* 18 months. May be stored at room temperature.

## KENACORT®

**Tablets**

Squibb Triamcinolone

Kenacort, Squibb Triamcinolone, is the 9-alpha-fluoro-16-alpha-hydroxy derivative of prednisolone. Besides being a potent anti-inflammatory, antirheumatic and anti-allergic agent, Kenacort differs from other glucocorticoids in some aspects of its clinical utility. For example, in the usual doses, it rarely causes sodium or fluid retention; voracious appetite and its associated weight gain, common with some glucocorticoids, are very unusual with Kenacort. Thus, for patients in whom such side effects are to be avoided, Kenacort may be the drug of choice. Psychic stimulation does not usually occur and patients in whom other steroids have induced euphoria or mental stimulation would not be likely to experience the same effects with Kenacort.

Kenacort, as with other newer corticosteroids, appears to persist in the blood for a longer time than hydrocortisone (cortisol).

Plasma biologic half-life of injected steroid *(in minutes)*

| *Corticosteroid* | Man[1] | Man[2] | Dog[3] |
|---|---|---|---|
| Hydrocortisone | 101 | 120 | 44-52 |
| Prednisolone | 200 | 180 | 60-71 |
| Methylprednisolone | — | 210 | 80.9 |
| Dexamethasone | 200 | — | 60 |
| Triamcinolone | >300 | — | 116.7 |

[1] *Melby J. C.: Med. Clin. North America* 45: 875 *(July)* 1961.
[2] *McGavack, T. H.: Nebraska J. Med.* 44: 377 *(Aug.)* 1959.
[3] *Florini, J. R. et al.: J. Pharmacol. and Exper. Therap.* 131: 287. *(Mar.)* 1961.

Historically, corticoids have been administered on a t.i.d. or q.i.d. basis. In clinical studies, Kenacort has proved efficacious even when longer intervals between doses were employed. Single daily doses of Kenacort have been used effectively in the dermatoses, allergic disorders, and mild connective tissue diseases (acute bursitis, myositis, fibrositis, etc.). In rheumatoid arthritis, the incidence of effective control using the single daily dose was considerably lower, but occurred often enough to make the regimen worthy of trial in this condition. Divided dosage with Kenacort continues to be effective for many other patients with corticosteroid-responsive conditions.

*Advantages:*

* effective anti-inflammatory, antirheumatic and anti-allergic action
* sodium or fluid retention rare

* secondary hypertension rare; blood pressure often reduced to normal
* undesirable psychic stimulation does not usually occur
* voracious appetite unusual
* no need for dietary salt restriction

*Indications:* Bronchial asthma, other allergic disorders, dermatoses, psoriasis (except mild, uncomplicated), nephrotic syndrome, pulmonary emphysema, pulmonary fibrosis, acute rheumatic fever, vasomotor rhinitis, urticaria, angioneurotic oedema, rheumatoid arthritis, the lymphatic leukaemias, lymphosarcoma, Hodgkin's disease, disseminated lupus erythematosus. In other forms of leukaemia where, for example, haemolytic anaemia or thrombocytopenia occur, Kenacort may be helpful. It should be emphasized that steroid therapy for the lymphomata is palliative. Kenacort is also useful in patients with congestive heart failure resistant to diuretics, and has been used successfully in acute bursitis, sprue, uveitis—and such blood dyscrasias as chronic eosinophilia, thrombocytopenic purpura and haemolytic anaemia. The drug may also be of value when other corticosteroids have failed or have reached a limit of usefulness in steroid-responsive conditions.

*Contraindications:* Although corticosteroids have been used experimentally in the treatment of active tuberculosis, the disease, whether active, latent or healed is still usually considered a *contraindication* to their use. Corticoids are also contraindicated in ocular herpes simplex and acute psychosis, and relatively so in presence of active peptic ulcer, acute glomerulonephritis, and infections which cannot be controlled by antibiotics. The use of steroids in patients with myasthenia gravis may aggravate myasthenic symptoms and should, therefore, be given with proper precautions. Corticosteroids are not recommended for pregnant patients, particularly during the first trimester, except when the disease for which they are indicated is very severe. In newborns of mothers who have received corticoid therapy, the possible occurrence of hypoadrenalism should be borne in mind. When considering triamcinolone treatment in the presence of any of the following, the need for steroid therapy must be thoroughly weighed against the possible deleterious effects on the contraindicated condition; diverticulitis, fresh intestinal anastomoses, thrombophlebitis, psychotic tendencies, chronic nephritis, metastatic carcinoma, osteoporosis, and history of peptic ulcer.

*Adverse Reactions and Precautions:* Triamcinolone, like all potent steroids, should be used under close clinical supervision. Weight gain, oedema and hypertension, the usual unwanted steroid effects, usually do not occur; patients must be observed for the less obvious undesirable effects. All corticosteroids may mask symptoms of infection and permit spread of an invading organism. If questionable findings are encountered it may be advisable to interrupt triamcinolone therapy until an accurate diagnosis is made.

In acute and chronic *bacterial* infections, triamcinolone should only be used in conjunction with suitable antibiotic or chemotherapeutic agents. The drug should be withheld during acute *viral* infections, such as ocular herpes simplex and varicella. Steroid patients must be watched carefully for the development of osteoporosis and spontaneous fracture, peptic ulcer or epigastric distress. Cushingoid changes such as facial rounding, buffalo hump and other signs of fat deposition may be seen in some cases. Purpura, flushing of the face, sweating, acne,

striae, hirsutism, vertigo and headache may be encountered. The growth-suppressing effects of corticosteroids in children should be considered when triamcinolone is administered to the paediatric age group.

Thromboembolism, aseptic necrosis of the hip, necrotizing angiitis, acute pancreatitis and ulcerative oesophagitis are other possible side effects of steroid therapy.

*A liberal protein intake is essential* for patients receiving triamcinolone, since it does not stimulate appetite. On prolonged therapy, most patients have a tendency to gradual weight loss, sometimes associated with negative nitrogen balance. As with all corticoids, wasting and weakness of skeletal muscle may occur in some patients. Anabolic steroids appear to be useful in maintaining nitrogen equilibrium. Diabetic patients frequently require an increase in insulin dosage; latent diabetes mellitus may become manifest during steroid therapy.

While in rare instances increased intracranial pressure and papilloedema have been reported to occur after administration of corticosteroids, including triamcinolone, the mechanism of action has not been elucidated. The possible association of posterior subcapsular cataracts with the administration of high dosage, long-term systemic corticotherapy has been presented in the literature. For this and other reasons, long-term administration of corticoids should be kept at minimum dosage levels.

In therapeutic doses, glucocorticoids depress the function of the adrenal cortex. To avoid adrenal insufficiency, therapy should be withdrawn gradually (2 mg. every two to three days), particularly when patients are receiving large doses or prolonged treatment. Undue stress, i.e., surgery, trauma, severe illness, during or within a year after triamcinolone treatment has been terminated calls for prompt institution of adequate supportive measures for the duration of the stress. During treatment Kenacort dosage should be increased temporarily; supportive measures in the year after treatment should include ACTH and, in some situations of severe stress, hydrocortisone or cortisone.

*Dosage:* Individual requirements and the disease under treatment determine Kenacort dosage. A single daily dose, given either in the morning or at bedtime depending on the clinical situation, may be satisfactory for initial or maintenance therapy in many patients; others will require a divided daily dosage regimen such as b.i.d. to q.i.d. administration. Initial daily dosage generally ranges from 8 to 32 mg. for adults, and from 4 to 12 mg. for children under 25 Kg. Children over 25 Kg. may be given adult dosage. It may be necessary to administer initial adult dosage in children under 25 Kg. After a satisfactory response, the adult dosage is reduced *gradually* by 2 mg., every two to three days, to the optimal maintenance level. Maintenance dosage in children is regulated in terms of clinical response.

Intermittent Kenacort therapy employing other dosage intervals has been successful in the nephrotic syndrome, and this use has also been reported in the management of juvenile rheumatoid arthritis and in certain chronic dermatoses. In addition to patient convenience, it has been suggested that once daily administration of a corticosteroid is less likely to interfere with diurnal rhythm of the spontaneously secreting adrenal gland; if this is the reason for single daily dose therapy, the dose should be given in the morning. In other patients, i.e., the

arthritic who complains of morning stiffness, or the asthmatic who needs protection during the night, a nocturnal dose would be more desirable.

The 8 mg. tablet suggests an added convenience for those patients responsive to once-a-day or other intermittent oral Kenacort dosage.

*Patient transfers from other corticosteroids.* Initially, substitute 4 mg. Kenacort for each of the following:

25 mg. cortisone
20 mg. hydrocortisone
5 mg. prednisone
5 mg. prednisolone
4 mg. methylprednisolone
0.75 mg. dexamethasone
2 mg. paramethasone

Thereafter, dosage should be adjusted according to individual response.

KENACORT THERAPY GUIDE

| *Condition* | *Initial Daily Dosage* | *Maintenance Daily Dosage* |
|---|---|---|
| bronchial asthma | adults:[1] 8-16 mg.<br>children: 8-12 mg. | adults: 2-8 mg.<br>children: 1-4 mg. |
| allergic disorders | adults:[1] 8-16 mg.<br>children: 4-8 mg. | adults: 4-16 mg.<br>children: 2 mg. or less |
| dermatoses[2] | adults:[1] 8-20 mg.<br>children: 4-12 mg. | adults and children:<br>2 mg. or less |
| psoriasis,[3] acute exacerbations | adults: 4-32 mg.<br>(advocated for short-term control only) | adults: 1-16 mg. |
| nephrotic syndrome | adults and children:<br>20-48 mg. to diuresis<br>(usually within 7-10 days) | adults and children:<br>intermittent therapy<br>8-16 mg. for 3 consecutive days per week. |
| pulmonary emphysema, pulmonary fibrosis[4] | adults: 8-32 mg. | adults: 1-4 mg. |
| rheumatic fever (acute) | in divided doses<br>adults: 16-20 mg.<br>children: 8-10 mg. | adults and children:<br>gradually reduce, discontinue |
| vasomotor rhinitis | adults: 8-16 mg.<br>children: 4-8 mg. | adults: 1-4 mg.<br>children: reduce, discontinue |

| *Condition* | *Initial Daily Dosage* | *Maintenance Daily Dosage* |
|---|---|---|
| urticaria | adults[1] and children: 12-20 mg. for 5 days | |
| angioneurotic oedema | adults: 8-16 mg. | adults: gradually reduce |
| rheumatoid arthritis | adults[1a] and children: 4-12 mg. | adults: lowest adequate dose<br>children: individualized |
| lymphomatous diseases: chronic lymphatic leukaemia | adults and children: 32-60 mg. | adults and children: 2-24 mg. |
| acute lymphatic leukaemia | children: 1 mg./Kg. body weight | same as initial dosage |
| lupus erythematosus, disseminated; other collagen diseases | adults and children: 20-32 mg. | adults and children: 4-20 mg. |
| acute connective tissue diseases (acute bursitis, myositis, fibrositis, etc.) | adults: [1] 8-16 mg. | adults: 1-8 mg. |
| uveitis | adults: 24-32 mg. | adults: gradually reduce |
| sprue | adults: 12-24 mg.<br>children: 3 mg. or more | adults and children: gradually reduce |

[1] Single daily doses have been effectively employed.

[1a] A single daily dosage regimen may be tried. If response is not satisfactory, daily dosage should be given in divided amounts. If no response is observed within 7 days, consideration should be given to the possibility of an erroneous diagnosis.

[2] For some chronic dermatoses, an alternate-day dosage regimen, using doses equivalent to daily dosage, may be effective. *Severe pemphigus requires high initial doses, even upto* 100 *mg. daily in divided doses.*

[3] Potent systemic steroids are not recommended for mild, uncomplicated psoriasis. Psoriasis recurs when medication is discontinued and may be more severe due to rebound phenomenon.

[4] *Appropriate antibiotic therapy must be given simultaneously.*

*Supply:*

Scored tablets: 1 mg., boxes of 100 (10 strips of 10's)
4 mg., boxes of 100 (10 strips of 10's)
8 mg., boxes of 48 (8 strips of 6's)

*Note:* Store at room temperature.

## KENACORT® INJECTION 10 mg. Parenteral Suspension

Squibb Triamcinolone Acetonide Aqueous Suspension

(Not for Intravenous Use)

Kenacort Injection is a synthetic corticoid with marked anti-inflammatory action. It is available as a sterile aqueous suspension, each ml. providing 10 mg. triamcinolone acetonide, with sodium chloride for isotonicity, 0.9% benzyl alcohol as a preservative, 0.75% sodium carboxymethylcellulose, and 0.04% polysorbate 80.

*Action and Uses:* The preparation is intended for intra-articular, intrasynovial, or intrabursal injection in the treatment of the pain and inflammation of joints, bursae, and tendon sheaths and for intralesional (intradermal and sometimes subcutaneous) injection in the management of a variety of localized dermatoses.

*Intra-articular:* The drug provides valuable local therapy of joint pain arising from such conditions as rheumatoid arthritis, osteoarthritis, tendinitis, synovitis, bursitis, and other conditions amenable to local corticosteroid injections. It offers freedom from systemic action, particularly when injections are given adjunctively in the management of the arthritides. According to clinical reports, the preparation has produced good to excellent results in the vast majority of patients.

Relief of pain and swelling, and greater freedom of motion are usually obtained within a few hours after injection; amelioration of symptoms may be permanent or sustained over a period of one to several weeks. Kenacort frequently provides substantial, long-lasting benefits where previously administered corticosteroid, such as hydrocortisone or the prednisteroids, afforded only partial or transient relief. In processes, the preparation is intended to supplement other conventional therapeutic measures. Since intra-articular administrations, when given in the usual dosage range, do not produce physiologic hormonal effects, the drug is of particular value when systemic steroid therapy is contraindicated in these conditions. For localized conditions such as traumatic arthritis or bursitis, intra-articular administration may be the sole therapy required. Moreover, side effects such as painful local reactions which have occurred with intra-articular use of other corticosteroids have been rare following injection of triamcinolone acetonide.

*Intradermal:* Injection of the drug directly into localized lesions of many dermatologic conditions produces a relatively prompt involution and rapid relief of pruritus. Intradermal administration is often effective where topical corticosteroid applications have failed, and may produce prolonged remissions where topical steroids have effected only temporary relief. Moreover, this procedure avoids the systemic effects which may accompany oral or parenterally administered corticosteroids. Clinical results obtained with this preparation recommend its use for the localized, hypertrophic, infiltrated, inflammatory lesions of such conditions as lichen simplex chronicus (neurodermatitis), psoriatic plaques, granuloma annulare, lichen planus, certain keloids, and alopecia (areata and totalis).

*Contraindications:* The use of corticosteroids is contraindicated in the presence of local or systemic viral infection, tuberculosis of the skin, or any active infection in

or near joints or dermatologic lesions. The preparation should not be used to alleviate joint pain arising from infectious states such as gonococcal or tuberculous arthritis.

*Warning: Because it is a suspension, the preparation should not be administered intravenously. Strict aseptic technique is mandatory.*

*Precautions:* Although therapy with Kenacort Injection will ameliorate symptoms, it is in no sense a cure and the hormone has no effect on the cause of the inflammation. Therefore, this method of treatment does not obviate the need for the conventional measures usually employed. *With intra-articular administration the inadvertent injection of the suspension into the soft tissues surrounding a joint is not harmful, but may lead to the occurrence of systemic effects and is the most common cause of failure to achieve the desired local results.*

A marked increase in pain accompanied by local swelling, further restriction of joint motion, fever, and malaise are suggestive of a septic arthritis. If these complications should appear, and the diagnosis of sepsis is confirmed, antimicrobial therapy should be instituted immediately and continued for 7 to 10 days after all evidence of infection has disappeared.

Following intra-articular steroid therapy, patients should be specifically warned to avoid over-use of joints in which symptomatic benefit has been obtained. Negligence in this matter may permit an increase in joint deterioration that will more than offset the beneficial effects of the steroid.

Unstable joints should not be injected. Repeated intra-articular injection may in some cases result in instability of the joint. Injections are given, X-ray follow-up is suggested.

Unlike other corticosteroids, triamcinolone and its derivatives do not stimulate appetite; during prolonged therapy, *a liberal protein intake is essential* and administration of anabolic steroids may be useful for counteracting the tendency to gradual weight loss sometimes associated with negative nitrogen balance, wasting and weakness of skeletal muscles.

Since rare cases of anaphylactoid reactions following parenteral triamcinolone therapy have been reported, appropriate precautions are advised.

In females past menarche, menstrual irregularities (amenorrhoea, intermenstrual spotting, or prolonged bleeding) can occur; this possibility should be mentioned to the patient. It should also be borne in mind that triamcinolone acetonide, like other glucocorticoids, may aggravate diabetes, so that higher insulin dosage may become necessary; or, it may precipitate the manifestation of latent diabetes mellitus. Corticosteroids are not recommended for patients with myasthenia gravis, diverticulitis, fresh intestinal anastomoses, thrombophlebitis, psychotic tendencies, exanthematous diseases, chronic nephritis, metastatic carcinoma, osteoporosis, and history of peptic ulcer. In the presence of any of these conditions, the need for steroid therapy must be carefully weighed against the possible deleterious effects.

As with other corticosteroids, the possibility of other severe reactions should be considered. If such reactions should occur, appropriate corrective measures should be instituted and use of the drug discontinued.

*Side Effects:* Undesirable reactions following intra-articular administration of the preparation have included transient pain, occasional local irritation at the injection site, and occasional brief increase in joint discomfort; following intradermal administration, transient local discomfort and local atrophy (which usually disappears, unless the basic disease process is itself atrophic) have occurred.

Since systemic absorption may occasionally occur with intra-articular or other local administration, patients should be watched closely for side effects associated with any corticosteroid therapy. These include relative adrenocortical insufficiency (particularly in times of stress due to trauma, surgery, or severe illness), hyperglycaemia, glycosuria, aggravation or masking of infection, osteoporosis (reversible only with difficulty), spontaneous fractures, aseptic necrosis of the hip, myopathy, weakness, activation and complication of peptic ulcer including perforation and haemorrhage, acute pancreatitis, ulcerative oesophagitis, moon face, buffalo hump, abnormal fat deposits, acne, striae, hirsutism, flushing of the face, sweating, menstrual irregularities, petechiae and purpura, necrotizing angiitis, growth-suppression in children, thromboembolism, insomnia, psychic disturbances (particularly mild depression, in contrast to the euphoria seen with other glucocorticoids), vertigo, headache, increased intracranial pressure, papilloedema, posterior subcapsular cataracts (occasionally requiring extraction), and rarely, oedema, hypertension, syncopal episodes, and anaphylactoid reactions.

When adverse reactions do occur, they are usually reversible and disappear when the hormone is discontinued.

*Administration and Dosage:* Shake the vial before use to insure a uniform suspension. After withdrawal, inject without delay to prevent settling in the syringe. Careful technique should be employed to avoid the possibility of entering a blood vessel or of introducing infection.

*Intra-articular:* Dosage depends on the size of the joint and the severity of symptoms. Doses of 2.5 to 5 mg. *for smaller joints* and 5 to 15 mg. *for larger joints* have usually been sufficient to palliate symptoms. Single injections for multiple joint involvement of up to a total of 20 mg. or more have been given without incident.

Dosage may be increased if initial results are inadequate or too transient. A single injection frequently affords complete remission of symptoms. However, several injections may be needed for satisfactory relief. Response to the preparation varies in duration. For some patients remission of symptoms is permanent, while others may require subsequent courses of therapy after periods of relief ranging from one week to several months. The duration of temporary remission is often considerably improved following a series of injections, and therapy should therefore be repeated on recurrence of symptoms, and not at set intervals.

The use of a local anaesthetic may often be desirable. When a local anaesthetic is used with Kenacort Injection, the anaesthetic package insert should be read with

care and all the precautions connected with its use should be observed. It should be injected into the surrounding soft tissues prior to the intra-articular injection. A small amount may also be instilled into the joint. If an excessive amount of synovial fluid is present in the joint, some, but not all should be aspirated to aid in the relief of pain and to prevent undue dilution of the steroid. Then the usual intra-articular injection technique, as described in standard text books should be followed. For treatment of ganglia, Kenacort Injection is injected directly into the cyst cavity. In treating such conditions as tendinitis, tenosynovitis, or trigger finger, care should be taken to insure that the injection is made into the tendon sheath rather than into the tendon substance. Conditions such as peritendinitis, tennis elbow, frozen shoulder, rheumatoid nodules, fibrositis, and collateral ligament strains and sprains in the knee may be treated by infiltrating the preparation into the area of greatest tenderness.

*Intradermal:* The usual dose is 0.1 to 0.3 ml. depending on the size of the lesion. Whenever possible, the volume injected at any site should be limited to 0.1 ml.; multiple sites (separated by one centimetre or more) may be used if more than this is required. The multiple-site method of administration will tend to minimize local tissue intolerance and the occurrence of atrophy. The total volume administered at a session should probably not exceed 3.0 ml. bearing in mind that the greater the total volume employed the more corticosteroid becomes available for possible systemic absorption and subsequent systemic corticosteroid effects. Administration may be repeated, if necessary, at weekly or less frequent intervals. The preparation is injected directly into the lesion, i.e., intradermally or sometimes subcutaneously. For accuracy of dosage measurement and ease of administration, it is preferable to employ a tuberculin syringe and a small bore needle (23 to 25 gauge). Ethyl chloride spray may be used to ease the discomfort of injection.

*Supply:* 10 mg./ml., 1 ml. vials.

*Expiration date* 24 months.

## KENACORT® INTRAMUSCULAR 40 mg. Parenteral Suspension

Squibb Triamcinolone Acetonide Aqueous Suspension

(Not for Intravenous or Intradermal Use)

Kenacort Intramuscular is a sterile aqueous suspension providing a concentration of 40 mg. triamcinolone acetonide per ml. with sodium chloride for isotonicity, 0.9% benzyl alcohol as a preservative, 0.75% sodium carboxymethylcellulose, and 0.04% polysorbate 80. Triamcinolone acetonide is a synthetic corticosteroid with marked anti-inflammatory action which was developed at The Squibb Institute for Medical Research. Kenacort Intramuscular is primarily intended for depot intramuscular administration in those allergies, dermatoses, and arthritides for other connective tissue disorders which are benefited by systemic corticosteroid therapy. The preparation is also of value when local injection of a steroid is indicated for painful, inflammatory conditions in joints, bursae, tendon sheaths, or other localized areas, particularly when a high steroid concentration in a small volume is desirable.

*Action and Uses:* Clinical reports on the systemic use of Kenacort Intramuscular have indicated that it offers a significant advantage over orally administered corticosteroids, in that it need only be given intermittently, even in chronic conditions. In sharp distinction to oral corticosteroids, which usually are administered on a daily basis, Kenacort Intramuscular has an extended duration of effect. Following a single intramuscular dose of 40 to 80 mg. amelioration of symptoms may be permanent or sustained over a period of several weeks.

The intramuscular dosage of triamcinolone acetonide, calculated on a per-day basis is about 1 to 3 mg. which is considerably less in, many instances than the amount of steroid required with oral administration of triamcinolone. In a study of triamcinolone preparations given intramuscularly for rheumatoid arthritis one investigator reported that in approximately, 25% of his patients the intramuscular maintenance dose, calculated on the basis of its daily equivalent, was smaller than the oral dose which the patients had previously required. Other clinical studies suggest that gastrointestinal side effects may be reduced when intramuscular steroid therapy is instituted in place of oral therapy.

A significant number of patients, particularly those with allergic disorders, have experienced a prolonged remission of symptoms following intramuscular injection of triamcinolone acetonide.

Studies indicate that following a single intramuscular dose of 60 to 100 mg. of triamcinolone acetonide, adrenal suppression occurs within 24 to 48 hours and then gradually returns to normal usually in 30 to 40 days. This finding correlates closely with the extended duration of therapeutic action achieved with the drug.

The local injection (such as intra-articular) of Kenacort Intramuscular also has a prolonged effect in the majority of patients. Improvement in motion and relief of pain and swelling which may be obtained within a few hours, are frequently sustained over a period of several weeks, and, in self-limited disorders, may be permanent. The freedom from systemic action following intra-articular injection is a particularly desirable attribute, especially when this mode of therapy is employed as an adjunct in the management of the arthritides. Kenacort frequently provides substantial, long-lasting benefits where previously administered corticosteroids, such as hydrocortisone or the prednisteroids, afforded only partial or transient relief. Moreover, the side effects such as painful local reactions which have occurred with intra-articular use of other corticosteroids have been rare following injection of triamcinolone acetonide.

The intramuscular administration of Kenacort Intramuscular is indicated for systemic corticosteroid therapy in such conditions as allergic diseases, dermatoses, or generalized rheumatoid arthritis and other connective tissue disorders. Intramuscular administration is particularly valuable in such conditions when oral corticosteroid therapy is not feasible.

Kenacort Intramuscular may also be given by intra-articular or intrabursal administration, and by injection into tendon sheaths or ganglia, in the treatment of local inflammatory conditions when symptoms are severe enough to require higher-than-usual dosage. This route of administration affords valuable local therapy of pain, swelling, and stiffness arising from such conditions as traumatic

or rheumatoid arthritis, osteoarthritis, synovitis, bursitis and tendinitis. The preparation should not be injected into "trigger points" unless injection is made into the musculature and not in overlying fat.

In the management of generalized arthritic disease, the intra-articular injection of triamcinolone acetonide is intended to supplement other conventional therapeutic measures. Since intra-articular administration, when given in the usual dosage range, generally does not produce physiologic hormonal effects, the preparation is of particular value when systemic steroid therapy is contraindicated in these conditions. For localized conditions such as traumatic arthritis or bursitis, intra-articular administration may be the sole therapy required.

*Contraindications:* The use of corticosteroids is contraindicated in the presence of herpes simplex of the eye and in acute psychosis. Although corticosteroids have been used in the treatment of chickenpox and, experimentally, in the treatment of tuberculosis, these diseases are usually considered as contraindications. The use of corticosteroids is contraindicated in the presence of local or systemic viral infection, tuberculosis of the skin, or any active infection in or near joints or dermatologic lesions. The preparation should not be used to alleviate joint pain arising from infectious states such as gonococcal or tuberculous arthritis.

*Warning: Because it is a suspension the preparation should not be administered intravenously. Strict aseptic technique is mandatory. The preparation is not recommended for children under six years of age.*

*Precautions:*

*Following Administration by Any Route:*
Kenacort Intramuscular should be administered only with full knowledge of characteristic activity of, and varied responses to, adrenocortical hormones. Like other potent corticosteroids, triamcinolone acetonide should be used under close clinical supervision. The increase in weight, oedema and hypertension which constitute the usual early unwanted steroid effects generally do not occur with triamcinolone acetonide; thus patients must be carefully observed for less obvious signs. Unlike other corticosteroids, triamcinolone and its derivatives do not stimulate the appetite; during prolonged therapy, *a liberal protein intake is essential*, and administration of anabolic steroids may be useful, for counteracting the tendency to gradual weight loss, sometimes associated with negative nitrogen balance and wasting or weakness of skeletal muscles.

Triamcinolone acetonide is not an agent of choice in the treatment of adrenocortical insufficiency. When bacterial infections (local infections other than at the site of injection, or systemic infections) are present, therapy with triamcinolone acetonide is not recommended, but may be employed with caution and only in conjunction with appropriate antibiotic or chemotherapeutic medication.

Corticosteroids are not recommended for pregnant patients, particularly in the first trimester, except when the disease for which they are indicated is very severe. In new-borns of mothers who have received corticosteroid therapy the possible occurrence of hypoadrenalism should be borne in mind. Triamcinolone acetonide, like other glucocorticoids, may aggravate diabetes, so that higher insulin

dosage may become necessary or, it may precipitate the manifestation of latent diabetes mellitus.

Corticosteroids are not recommended for patients with myasthenia gravis, diverticulitis, fresh intestinal anastomoses, thrombophlebitis, psychotic tendencies, exanthematous diseases, chronic nephritis, metastatic carcinoma, osteoporosis, and history of peptic ulcer. In the presence of any of these conditions, the need for steroid therapy must be carefully weighed against possible deleterious effects. In the case of peptic ulcer, recurrence may be asymptomatic until perforation or haemorrhage occurs. Therefore, X-rays should be taken when therapy is prolonged or when there is any indication of gastric distress.

As with other corticosteroids, the possibility of other severe reactions should be considered. If such reactions should occur, appropriate corrective measures should be instituted and use of the drug discontinued.

Continued supervision of the patient after termination of triamcinolone acetonide therapy is essential, since there may be a sudden reappearance of severe manifestations of the disease for which the patient was treated.

*Following Intramuscular Administration:*
Unless a deep intramuscular injection is given, local atrophy is likely to occur. (For recommendations on injection techniques, see *Administration and Dosage.*) Due to the significantly higher incidence of local atrophy when the material is injected into the deltoid area, this injection site should be avoided in favour of the gluteal area. Only very unusual circumstances would warrant injection into the deltoid area.

Menstrual irregularities may occur, and this possibility should be mentioned to female patients past menarche.

Adrenal insufficiency is not likely to be a problem when intramuscular therapy is terminated but this possibility should be borne in mind. Patients on long-term systemic therapy with triamcinolone acetonide may require supportive corticosteroid therapy in times of stress (such as trauma, surgery, or severe illness) both during the treatment period and for a year afterwards.

*Following Intra-articular Administration:*
Although therapy with Kenacort Intramuscular will ameliorate symptoms, it is in no sense a cure and the hormone has no effect on the cause of inflammation. Therefore, this method of treatment does not obviate the need for the conventional measures usually employed. *The inadvertent injection of the suspension into the soft tissues surrounding a joint is not harmful, but may lead to the occurrence of systemic effects, and is the most common cause of failure to achieve the desired local results.*

Following intra-articular steroid therapy, patients should be specifically warned to avoid over-use of joints in which symptomatic benefit has been obtained. Negligence in this matter may permit an increase in joint deterioration that will more than offset the beneficial effects of the steroid.

Unstable joints should not be injected. Repeated intra-articular injection may in

some cases result in instability of the joint. In selected cases, particularly where repeated injections are given, X-ray follow-up is suggested.

An increase in joint discomfort has seldom occurred. A marked increase in pain following intra-articular injection accompanied by local swelling, further restriction of joint motion, fever, and malaise, may indicate a septic arthritis. If the diagnosis of septic arthritis is confirmed, administration of triamcinolone acetonide should be stopped; and antimicrobial therapy should be instituted immediately and continued for 7 to 10 days after all evidence of infection has disappeared.

*Side Effects:*

*Following Administration by Any Route:*
Since side effects due to systemic absorption may occur (even with local administration, and particularly with doses of 40 mg. or higher), patients should be watched closely for side effects associated with any corticosteroid therapy. These include relative adrenocortical insufficiency (particularly in time of stress due to trauma, surgery, or severe illness; or after cessation of therapy with triamcinolone acetonide—see *Precautions*), hyperglycaemia, glycosuria, aggravation or masking of infection osteoporosis (reversible only with difficulty), spontaneous fractures, aseptic necrosis of the hip, myopathy, weakness, activation and complication of peptic ulcer including perforation and haemorrhage, acute pancreatitis, ulcerative oesophagitis, moon face, buffalo hump, abnormal fat deposits, acne, striae, hirsutism, flushing of the face, sweating, menstrual irregularities (amenorrhoea, intermenstrual spotting, or prolonged bleeding), petechiae and purpura, necrotizing angiitis, growth-suppression in children, thromboembolism, insomnia, psychic disturbances (particularly mild depression in contrast to the euphoria seen with other corticosteroids), vertigo, headache, increased intracranial pressure, papilloedema, posterior subcapsular cataracts (occasionally requiring extraction), and rarely, oedema, hypertension, syncopal episodes and anaphylactoid reactions.

When adverse reactions do occur, they are usually reversible and disappear when the hormone is discontinued.

*Following Intramuscular Administration:*
Severe pain has been reported in a few cases. Abscess formation and local depigmentation have also occurred.

*Following Intra-articular Administration:*
Undesirable reactions have included transient pain, occasional local irritation at the injection site, local depigmentation, and occasional brief increase in joint discomfort.

*Administration and Dosage:* Shake the vial before use to insure a uniform suspension. After withdrawal, inject without delay to prevent settling in the syringe. Careful technique should be employed to avoid the possibility of entering a blood vessel or introducing infection.

*Systemic Dosage:* 60 mg. is the suggested initial dose for adults and children over

12, injected deep into the gluteal muscle. Subcutaneous fat atrophy may occur if care is not taken to inject the preparation intramuscularly. Dosage is usually adjusted within the range of 40 to 80 mg., depending upon patient response and duration of relief. However, some patients may be well controlled on dosage as low as 20 mg. or less. Patients with hay fever or pollen asthma who are not responding to pollen administration and other conventional therapy may obtain a remission of symptoms lasting throughout the pollen season after one injection of 40 to 100 mg.

The suggested initial dose for children from 6 to 12 years of age, is 40 mg. although dosage depends more on the severity of symptoms than on age or weight. There is insufficient clinical experience with Kenacort Intramuscular to recommend its use in children under 6 years of age.

Since duration of effect is variable, subsequent doses of Kenacort Intramuscular for adults and children should be given when signs and symptoms recur, and not at set intervals.

*Systemic Administration:* For systemic therapy with Kenacort Intramuscular, injection should be made deeply into the gluteal muscle to insure intramuscular delivery (see *Precautions*). For adults, a minimum needle length of 1½ inches is recommended. In obese patients, a longer needle may be required. Use alternate sites for subsequent injections.

*Local Dosage:* For intra-articular or intrabursal administration, and for injection into tendon sheaths or ganglia, dosage of Kenacort Intramuscular is dependent on the severity of symptoms and on the size of the joint of other localized area to be treated. For adults, doses upto 10 mg. for smaller areas and up to 40 mg. for larger areas have usually been sufficient to alleviate symptoms.

Single injections into several joints for multiple locus involvement up to a total of 80 mg., have been given without undue reactions. A single local injection of triamcinolone acetonide is frequently sufficient, but several injections may be needed for adequate relief of symptoms. Duration of relief is variable. For some patients, remission is permanent following 1 to 2 injections; for others, subsequent courses of therapy may be required after periods of relief ranging up to several months. The duration of temporary remission is often considerably lengthened following subsequent injections. Therapy should be repeated on recurrence of symptoms and not at set intervals.

*Local Administration:* With intra-articular or intrabursal administration, and with injection of Kenacort Intramuscular into tendon sheaths or ganglia, the use of a local anaesthetic may often be desirable. When a local anaesthetic is used, its package insert should be read with care and all the precautions connected with its use should be observed. It should be injected into the surrounding soft tissues prior to the local injection of the corticosteroid. A small amount of the anaesthetic solution may also be instilled into the joint. If an excessive amount of synovial fluid is present in the joint, some but not all, should be aspirated to aid in the relief of pain and to prevent undue dilution of the steroid. The usual injection technique as described in standard textbooks, should then be followed. For treatment of ganglia, Kenacort Intramuscular is injected directly into the cyst

cavity. In conditions such as tendinitis, tenosynovitis, or trigger finger, care should be taken to insure that the injection is made into the tendon sheath and not into the tendon substance. Such conditions as peritendinitis, tennis elbow, frozen shoulder, rheumatoid nodules, fibrositis, and collateral ligament strains and sprains in the knee may be treated by infiltrating Kenacort Intramuscular into the area of greatest tenderness.

For other uses, a more dilute form of triamcinolone acetonide is available.

*Supply:* 40 mg./ml., 1 ml. vials.

*Expiration date* 24 months.

## KENADERMA®

**Ointment**

Squibb Triamcinolone Acetonide with Halquinol (Quixalin®)

Kenaderma combines the well-proven topical corticosteroid, triamcinolone acetonide with halquinol (Quixalin).

Kenaderma contains:

| | |
|---|---|
| Triamcinolone acetonide | 0.025% |
| Halquinol (Quixalin) | 0.75 % |

In Kenaderma the well-proven topical corticosteroid, triamcinolone acetonide is combined with halquinol. Because corticosteroid therapy increases the risk of secondary infection, particularly in skin lesions likely to be scratched, Kenaderma is recommended for all dermatoses whether they are infected or not.

*Rationale:* With the increasing awareness of antibiotic sensitivity and the risk of producing antibiotic-resistant organisms in patients being treated with topical preparations, there is much to be said for the use of an efficient chemotherapeutic agent in dermatological preparations.

Halquinol is such a chemotherapeutic agent with the additional benefit of a wider spectrum, being active against all common skin pathogens, including fungi and yeasts.

Dermatologists are becoming increasingly aware of subclinical infection in the common skin diseases such as eczema. Kenaderma with its powerful chemotherapeutic agent halquinol, covers this risk of hidden infection. The range of conditions which may be treated also includes intertrigo and pruritus ani where the antifungal activity of halquinol makes Kenaderma particularly suitable.

*Action:* Kenaderma provides rapid, complete, often prolonged relief of itching and burning in a wide variety of skin disorders. Kenaderma also prevents or combats secondary skin infections due to bacteria and fungi.

*Indications:* Kenaderma is indicated for the treatment of inflammatory dermatoses where topical corticosteroids would normally be used.

1. In infective conditions such as folliculitis and sycosis barbae the advantages of using Kenaderma are obvious with its antibacterial, antifungal and anti-inflammatory properties.

2. Eczemas as a group can be successfully treated with Kenaderma, especially when the real problem of masked or subclinical infection which so commonly occurs is considered.

   Kenaderma is indicated in:

   * infantile eczema and atopic eczema
   * napkin dermatitis
   * seborrhoeic dermatitis
   * varicose eczema
   * contact dermatitis
   * intertrigo
   * anogenital pruritus

3. Fungus diseases of the skin, including paronychia, where there is a degree of inflammatory reaction, may well benefit from the use of a potent corticosteroid combined with a powerful fungicide. Kenaderma covers these aspects and has the added advantages of being active against yeast infections which are so commonly the cause of chronic paronychia.

4. In chronic recalcitrant dermatoses where occlusive dressings are used in conjunction, e.g.,

   (a) chronic eczema and pompholyx
   (b) lichen planus
   (c) lichen simplex

*Advantages:*

* triamcinolone acetonide in Kenaderma is dramatically effective, giving rapid, complete and prolonged relief of itching, burning and inflammation
* halquinol in Kenaderma is consistently effective against most of the skin pathogens, both bacterial and fungal, including antibiotic resistant staphylococci
* halquinol in Kenaderma is not an antibiotic and to date skin sensitization has not been reported
* halquinol in Kenaderma is more active *in vitro* than other halogenated derivatives of oxine

*Side Effects:* Transient stinging may be experienced in a very small percentage of patients. A yellowish discoloration of the skin may occur with Kenaderma and clothing, especially cotton, may also be stained with Kenaderma but this is easily washed out. Sensitization has not yet been reported.

*Contraindications:* Kenaderma should not be used in the eye and care should be taken when applying the ointment near the eyes. Kenaderma is not indicated for treating primary skin infections like boils, infected wounds, etc. Kenaderma is

not indicated in tuberculosis and viral skin disorders.

*Supply:* Kenaderma is supplied in 5 Gm. collapsible tubes.

## KENALGESIC®

**Tablets**

Squibb Triamcinolone (Kenacort®) with Acetylsalicylic Acid

Each Kenalgesic Tablet contains Kenacort (Squibb Triamcinolone) 0.5 mg. and Acetylsalicylic Acid 325 mg.

*Action:* Kenalgesic combines the antiallergic and anti-inflammatory effects of the corticosteroid, triamcinolone with the analgesic and antipyretic actions of acetylsalicylic acid to achieve therapeutic effect with one convenient form.

*Indications:* Kenalgesic is indicated for the relief of pain and inflammation in conditions such as lumbago, sciatica, arthralgia, myalgia, neuralgia, pleurodynia, bursitis, menopausal arthritis and cervicobrachial neuritis. The uricosuric effect of acetylsalicylic acid along with the steroidal effect of Kenacort makes it valuable in gout.

It is useful in all forms of fibrositis including that which accompanies mild rheumatoid arthritis and osteoarthritis.

In the treatment of rheumatoid arthritis higher dosages may have to be given.

*Advantages:*

* dual action—analgesic and steroid effects
* convenient oral use
* widely-accepted acetylsalicylic acid supplements the superior corticosteroid, triamcinolone, which has significant advantage in reduced side effects over the other steroids. With triamcinolone there is absence of salt or water retention, no secondary hypertension, no excessive appetite and no mood changes

*Side Effects:* Kenalgesic is well tolerated. Side effects common to the steroid group (except oedema and euphoria, virtually eliminated with triamcinolone) may occur, though they tend to be infrequent and mild with the recommended doses. Dosage reduction usually controls such effects. All the usual contraindications to glucocorticoid therapy apply including active tuberculosis and bacterial infections (unless controlled by other medication), myasthenia gravis, active peptic ulcer, exanthematous eruptions and early pregnancy.

*Dosage:* Therapy should be individualized.

For the relief of pain and inflammation 2 tablets three times a day is usually sufficient.

For the treatment of rheumatoid arthritis higher dosage may be required (2 to 3 tablets 4 times a day).

When satisfactory control is obtained, gradually reduce the daily dosage to

minimum effective maintenance level. For the best results, administer after meals and at bedtime.

*Supply:* Boxes of 100 tablets (10 strips of 10's).

*Expiration date* 24 months.

*Note:* May be stored at room temperature.

## KENALOG-S® — Lotion, Ointment

Squibb Triamcinolone Acetonide with Neomycin-Gramicidin (Spectrocin®)

Kenalog-S combines the potent *anti-inflammatory, anti-allergic, antipruritic* action of triamcinolone acetonide with the wide spectrum *antibiotic* action of Spectrocin. It provides prompt, complete, often prolonged relief of itching, burning, inflamed skin lesions threatened or complicated by secondary bacterial infection.

Each ml. Kenalog-S Lotion supplies 1.0 mg. (0.1%) triamcinolone acetonide, 2.5 mg. neomycin base (as sulphate) and 0.25 mg. gramicidin.

Kenalog-S Ointment is available in two strengths: Kenalog-S 0.05% and Kenalog-S 0.1%.

Each gramme Kenalog-S 0.05% Ointment supplies 0.5 mg. (0.05%) triamcinolone acetonide, 2.5 mg. neomycin base (as sulphate) and 0.25 mg. gramicidin.

Each gramme Kenalog-S 0.1% Ointment supplies 1.0 mg. (0.1%) triamcinolone acetonide, 2.5 mg. neomycin base (as sulphate) and 0.25 mg. gramicidin.

* TRIAMCINOLONE ACETONIDE is clinically distinguished by its marked anti-inflammatory, anti-allergic, antipruritic effects. It produces good to excellent therapeutic results in the vast majority of patients. Paired comparison studies with 1.0% hydrocortisone and 0.5% prednisolone preparations have shown that triamcinolone acetonide in 0.1% concentration, usually acts faster and produces more dramatic, more consistent, and more complete therapeutic results. Moreover, triamcinolone acetonide is frequently effective in those instances where hydrocortisone and other topical steroids fail to bring about a good or complete therapeutic response.

* SPECTROCIN combines the broad spectrum activities of two potent topical antibiotics, neomycin and gramicidin. The joint actions of these powerful anti-infectives provide comprehensive antibacterial therapy against a wide range of gram-positive and gram-negative bacteria, including those responsible for most bacterial skin infections.

*Indications:* Kenalog-S is indicated in the following conditions when threatened or complicated by bacterial superinfection:

* atopic dermatitis
* contact dermatitis
* eczematous dermatitis
* infectious eczematoid dermatitis

* neurodermatitis
* seborrhoeic dermatitis
* insect bites
* lichen simplex chronicus
* stasis dermatitis
* nummular eczema
* infantile eczema
* anogenital pruritus

and other dermatoses amenable to topical corticosteroid-antibiotic therapy.

In exfoliative dermatitis and in localized eczematized lesions of psoriasis, Kenalog-S in conjunction with other indicated topical and/or systemic measures may be of value.

*Advantages:*

* four basic therapeutic effects—anti-inflammatory, anti-allergic, antipruritic, antibacterial
* dramatically effective—affords rapid, complete, often prolonged relief of itching, burning and inflammation
* frequently effective in those instances where hydrocortisone and other topical corticosteroids fail to bring about a good or complete therapeutic response
* a potent antibacterial preparation—combats or prevents bacterial infection
* well tolerated—systemic toxicity has not been observed, local intolerance to triamcinolone acetonide is rare: sensitivity reactions following the use of neomycin sulphate and gramicidin are seldom encountered.

*Administration:* Apply to the affected areas 2 to 3 times daily.

*Undesirable Effects:* Triamcinolone acetonide is extremely well tolerated. Systemic toxicity, such as oedema and electrolyte imbalance, has not been observed even though some patients were purposely given massive topical doses. Local intolerance to triamcinolone acetonide is rare—less than 1% in clinical studies of more than 2,000 patients. Sensitivity reactions following the use of Spectrocin (neomycin-gramicidin) are also seldom encountered.

*Supply:* Kenalog-S Lotion, 0.1%, 5 ml. plastic squeeze bottles.

*Expiration date* 18 months. Store in a cool place.

Kenalog-S Ointment, 0.05%, 5 Gm. tubes.

Kenalog-S Ointment, 0.1%, 2.5 Gm. and 5 Gm. tubes.

*Expiration date* 36 months. May be stored at room temperature.

## KENALOG-S® NASAL DROPS — Drops

Squibb Triamcinolone Acetonide, Neomycin-Gramicidin (Spectrocin®) with Phenylephrine

Kenalog-S Nasal Drops combines the potent anti-inflammatory corticosteroid triamcinolone acetonide and the dependable antibiotics neomycin and gramicidin (Spectrocin) with the effective local vasoconstrictor phenylephrine, for intranasal use in the management of inflammatory conditions involving the nasal passages and contiguous structures.

Kenalog-S Nasal Drops is available in a special plastic squeeze bottle designed to deliver a spray of approximately 0.1 ml. per squeeze.

Each ml. of Kenalog-S Nasal Drops provides:

Triamcinolone acetonide ..... 0.17 mg. (0.017%)
Neomycin base (as neomycin sulphate) ..... 3.5 mg.
Gramicidin ..... 0.05 mg.
Phenylephrine ..... 5 mg. (0.5%)
in scented aqueous vehicle.

*Action:* Triamcinolone acetonide aids in the reduction of capillary permeability and mucous membrane oedema by virtue of its anti-inflammatory and anti-allergic effects. The resultant relief of nasal congestion, with consequent improvement in ease of breathing, may be more prolonged than with the use of vasoconstrictors alone. The concentration of triamcinolone acetonide in the preparation is sufficient for good local activity and yet low enough to avoid systemic effects.

The two potent antibiotics, neomycin and gramicidin, are active against a wide range of pathogenic bacteria. Phenylephrine is one of the most commonly employed rapid-acting topical nasal vasoconstrictors. By shrinking the local tissues, it not only promotes easier breathing and better local drainage, but also permits other therapeutic agents to gain more complete access to the mucous membranes of the nasal and paranasal passages.

*Advantages:*

* rapidly clears nasal blockage of inflammatory/allergic origin
* 3-way therapy—marked corticosteroid/decongestant/antibiotic benefits ..

*—potent anti-inflammatory effects of a corticosteroid, Triamcinolone acetonide*

*—dependable antimicrobial activities—neomycin and gramicidin are highly active against a wide range of pathogenic bacteria*

*—proved vasoconstrictor activity—phenylephrine permits other therapeutic agents to gain more complete access to mucous membranes of nasal and paranasal passages*

*Indications:* Kenalog-S Nasal Drops is indicated, most often as adjunctive therapy in the management of acute or chronic, allergic or nonallergic inflammatory disease, and in those infections caused by organisms susceptible to neomycin and gramicidin, when the nasal passages and/or accessory nasal sinuses, or other contiguous structures (eustachian tubes, middle ear, nasopharynx) are involved. Other necessary measures may include environmental control, desensitization procedures, antihistamines, systemic corticosteroids or antibiotics, or other local procedures such as sinus irrigation or tubal insufflation. Such common conditions as seasonal or perennial allergic rhinitis, vasomotor rhinitis, and infectious rhinitis may be expected to be benefited.

*Contraindications:* Although the likelihood is minimal of systemic steroid effects resulting from the use of the nasal drops, it should be borne in mind that corticosteroids are contraindicated in the presence of active peptic ulcer, acute glomerulonephritis, herpes simplex of the eye, and infections that cannot be controlled with antibiotics. Topical steroid preparations are contraindicated in tuberculous, fungal and most viral lesions, herpes simplex, vaccinia and varicella particularly. The preparation is also contraindicated in patients with a history of hypersensitivity to any of its components.

*Side Effects and Precautions:* Phenylephrine when used intranasally is not likely to cause systemic effects. Sensitivity reaction to the antibiotics used is seldom a problem. Kenalog-S Nasal Drops is well tolerated and is not likely to cause any systemic toxicity such as oedema or electrolyte imbalance. In a few patients the nasal spray may induce local discomfort, such as a smarting sensation, pruritus or a feeling of dryness. Rebound congestion can be minimized by shorter period of use. In case of resistant infections or if secondary infection due to non-susceptible organisms appear, Kenalog-S Nasal Drops should be discontinued and/or other appropriate measures taken.

*Dosage:* The recommended dose for adults is 2 to 3 drops in each nostril, 3 to 5 times a day. For children (over six years), the dose is 1 to 2 drops in each nostril 3 to 5 times a day. Kenalog-S Nasal Drops is not recommended for children below six years.

*Administration:* Before using, shake the bottle gently. With the head upright, place the tip in the nostril and squeeze the bottle once while inhaling gently. Take out the tip from the nostril before releasing pressure. Repeat for the other nostril.

*Supply:* Kenalog-S Nasal Drops is supplied in special plastic squeeze bottles of 10 ml.

*Expiration date* 18 months.

## KENALOG-S® OPHTHALMIC OINTMENT — Ophthalmic Ointment

Squibb Triamcinolone Acetonide with
Neomycin-Gramicidin (Spectrocin®)

Kenalog-S Ophthalmic Ointment, Squibb Triamcinolone Acetonide with Neomycin-Gramicidin (Spectrocin) ophthalmic ointment provides, in each gramme, 1 mg. (0.1%) triamcinolone acetonide, neomycin sulphate equivalent to 2.5 mg. neomycin base, and 0.25 mg. gramicidin in Plastobase® Ophthalmic (Squibb Plasticized Hydrocarbon Gel) ointment base, for ophthalmic and otic use.

*Action:* Triamcinolone acetonide is clinically distinguished by its prompt and marked topical anti-inflammatory, anti-allergic, and antipruritic effects. When applied to the conjunctiva, it suppresses inflammatory reactions involving the anterior segment of the eye, inhibits vascularization and corneal scarring, controls ocular exudation, and relieves itching, smarting, and burning.

Neomycin and gramicidin combine the broad spectrum activities of two potent topical antibiotics. Neomycin is predominantly effective against staphylococci

and gram-negative organisms; gramicidin is included in the formulation chiefly for its activity against streptococci. Together they provide comprehensive antibacterial therapy or prophylaxis against a wide range of gram-positive and gram-negative organisms.

The ointment vehicle affords prolonged contact between the therapeutic agents and ocular or otic lesions. The ointment is particularly useful for night-time application in ophthalmic conditions, where its extended contact with affected tissue during the hours of sleep minimizes the need to wake the patient for administration of therapy.

Kenalog-S Ophthalmic Ointment is also suitably formulated for otic use. It controls inflammatory reactions involving the external ear and canal, reduces oedema, relieves pain and itching, inhibits exudation, and prevents or controls infection due to susceptible organisms.

*Advantages:*

* specifically for ophthalmic and otic use
* provides marked *anti-inflammatory*, *anti-allergic*, *antipruritic* and *antibacterial* effects
* triamcinolone acetonide is the clinically superior corticosteroid—dermatologic effectiveness topically is 40 times greater than hydrocortisone...10 times greater than dexamethasone
* rapidly relieves itching, redness, smarting and burning in the eye medically and postoperatively
* effectively treats inflamed, itching lesions of the external ear and auditory canal
* affords dependable broad spectrum antibiotic therapy and prophylaxis... provides in neomycin and gramicidin greater antibacterial depth of activity
* avoids the problem of sensitization in any future systemic treatment of more serious infections
* maintains homogeneity—even at warm temperatures, the base does not lose its suspending power

*Indications:* Kenalog-S Ophthalmic Ointment is indicated for inflammatory conditions involving the anterior segment of the eye, including nonpurulent blepharitis, acute nonpurulent conjunctivitis, iritis or iridocyclitis, episcleritis, superficial keratitis, and corneal traumas such as abrasions and burns. By virtue of the broad topical antibacterial spectrum provided by neomycin and gramicidin, the ointment is particularly useful in these inflammatory ocular conditions when bacterial infection threatens or is present. It is also indicated prophylactically or therapeutically following various ophthalmic surgical procedures such as cataract extractions and strabismus corrections.

The ointment is also indicated for various acute or chronic inflammatory conditions, either bacterial or noninfectious in origin, involving the external ear and auditory canal (otitis externa), e.g., seborrhoeic dermatitis and eczematous dermatitis.

*Contraindications:* Because the anti-inflammatory effects of corticosteroids may mask the signs of an infection and cause it to spread, the preparation is contraindicated

for the lesions of acute herpes simplex, vaccinia, vericella, and most other viral infections; tuberculous or fungal infections of the eye or ear; and acute purulent untreated conjunctivitis or blepharitis. The preparation is also contraindicated in those persons known to be hypersensitive to any of its components.

*Adverse Reactions and Precautions:* The preparation is generally well tolerated. Local irritation may occur in some patients. It is usually manifested as a transient burning sensation following instillation in the eye or ear.

Prolonged conjunctival application of topical corticosteroids may cause increased intraocular pressure in certain individuals. It is advisable that intraocular pressure be checked frequently when the preparation is so used.

In those diseases causing thinning of the cornea, perforation has occurred with the use of topical corticosteroids.

As with any antibiotic preparation, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. Constant observation of the patient is essential. Should superinfection occur, the preparation should be discontinued and/or appropriate therapy instituted.

*Dosage and Administration: Eye.* A ½ inch column of ointment should be applied to each affected eyelid two or three times daily. Since some ocular inflammations are prone to relapse, it is advisable to discontinue dosage gradually, maintaining close observation of the patient.

Patients should be instructed to take appropriate measures to avoid contaminating the applicator when applying the preparation.

If blurring of vision is to be avoided during working hours, it may be advisable to administer a solution formulation in the daytime, reserving the ointment for use at bedtime only.

*Ear.* If possible, clean the auditory canal thoroughly. A thin film of the ointment should be applied to the affected ear two or three times daily. A cotton-tipped applicator may be used if desired.

*Supply:* Tubes of 2.5 Gms. with ophthalmic tip.

*Expiration date* 24 months. May be stored at room temperature.

## KENAMINA® — Tablets

Squibb Triamcinolone and Carbinoxamine Maleate

Kenamina is a combination of triamcinolone—a potent corticosteroid with anti-inflammatory, anti-rheumatic and anti-allergic actions; and carbinoxamine maleate, a widely used, effective antihistamine. Each Kenamina Tablet contains 1.25 mg. triamcinolone and 2.0 mg. carbinoxamine maleate.

*Action:* Kenamina provides specific and effective treatment of allergic-pruritic

disorders. The combination of triamcinolone and carbinoxamine maleate, in which each component supplements the specific therapeutic action of the other, provides optimal therapeutic benefits with smaller effective doses of the steroid than would have been required with corticosteroid therapy alone, thus reducing the problem of side effects. Kenamina is therefore especially suitable for long-term therapy.

*Indications:* Kenamina is indicated for those allergic conditions in which antihistaminic and anti-inflammatory actions are desirable. These include allergic dermatoses, urticaria, angioneurotic oedema, pruritus, hay fever, vasomotor rhinitis, allergic conjunctivitis, drug and serum reactions, and certain cases of bronchial asthma.

*Advantages:* In a single preparation Kenamina provides:

* anti-inflammatory activity of triamcinolone (Kenacort)
* anti-histamine action of carbinoxamine maleate
* antipruritic as well as anti-allergic effect of both
* risk of side effects is considerably less with Kenamina than that produced by therapeutically equivalent dosages of either component alone

*Dosage:* The usual initial dose is one to two tablets orally. The dosage can be repeated at six hourly intervals. This dose should be adjusted to the individual requirements of the patient, with reduction to minimum maintenance level as improvement is obtained and discontinued as necessary.

*Contraindications:* As with other corticosteroids, triamcinolone should not be administered to patients with tuberculosis, active peptic ulcer, herpes simplex of the eye, exanthematous eruptions, or agitated psychotic states.

*Precautions:* Since drowsiness may occur while on this medication, extra care should be exercised in prescribing this to those who drive motor vehicles and those operating machinery. The physician must calculate the anticipated clinical improvement against the possibility of untoward effects before using this product in patients with cardiac failure, severe hypertension, diabetes mellitus, renal insufficiency, osteoporosis, or in patients with marked emotional instability and psychotic tendencies. Since triamcinolone may mask many signs of infection, the drug should not be administered until a diagnosis has been arrived at. Therapy should be discontinued if untoward effects are observed.

*Supply:* Boxes of 100 tablets (10 strips of 10's).

## LIVER INJECTION CRUDE, SQUIBB — Parenteral Solution

Liver Injection Crude, Squibb is a sterile aqueous solution preserved with 0.5 per cent phenol of that fraction of liver containing the anti-anaemic principle. It is a solution for intramuscular injection, available in 10 ml. vials. Each ml. contains Vitamin $B_{12}$ activity equivalent to 2 micrograms of cyanocobalamin. It is usually well tolerated and offers the advantage of being low in total solids and at the same time, comprising vitamins of B Complex in natural form and proportion.

*Indications:* Deficiency of anti-anaemic principle derived from liver appears to be common to all macrocytic anaemias. Liver Injection Crude, Squibb is effective in the treatment of all macrocytic anaemias and when combined with other therapy, it is a valuable adjunct in the management of patients intolerant to treatment with arsenicals and other heavy metal drugs and in the management of anaemias associated with pellagra, sprue, celiac disease, atrophic gastritis, cirrhosis of the liver, ulcerative colitis, roentgen illness, hyperemesis gravidarum, shock incident to severe thermal burns and lupus erythematosus. It provides a source of the unsynthesized members of vitamin B Complex for malnourished patients.

*Dosage and Administration:* Liver Injection Crude, Squibb is given by deep intramuscular injection into the buttocks. It is desirable to administer liver extract in excess of basic requirements in order to maintain a normal blood level and store reserve supply in the body. The clinical condition of the individual and the results of blood examinations are the criteria used to determine the adequacy of dosage employed. Dosage requirements vary from patient to patient and even in the same patient according to the stage of the disease.

As a routine 2 ml. daily until blood count is restored to normal will serve for mild cases of anaemia. Larger doses are generally required in markedly anaemic states, sprue, pellagra and other nutritional deficiencies characterised by intestinal manifestations. Administration of 5 to 7.5 ml. at appropriate intervals is recommended.

Therapeutic response to Liver Injection is best achieved with a well balanced diet with emphasis on proteins, vitamins and minerals.

*Supply:* Vials of 10 ml.

*Expiration date* 24 months.

*Note:* Should be stored in a cool place and protected from light.

## MAGNOMINT®

**Magma**

Squibb Mint-Flavoured Milk of Magnesia

Magnomint, an effective antacid and a mild laxative, is a smooth, creamy and homogenized milk of magnesia containing sodium citrate, saccharin and the special homogenizer, carageenin. It is distinguished by its deliciously different mint flavour.

*Advantages:*

* pleasant tasting—leaves no chalky, grity aftertaste
* made by a special homogenizing process which insures a smoother, creamier easy-to-take preparation—less likely to settle on standing
* as an antacid—usually effective in a matter of minutes
* as a laxative—relieves mild constipation

*Indications:* Antacid, mild laxative, sweetens the breath.

*Precautions:* Do not use any laxative when abdominal pain, nausea or vomiting are present. Frequent or prolonged use may result in dependence on laxatives.

*Dosage: Antacid*—Adults, 1 to 4 teaspoonfuls in ½ a glass of water, one or two hours after a meal or upon retiring. Children, ½ to 1 teaspoonful.

*Laxative*—Adults, 2 to 4 tablespoonfuls in ½ a glass of water, preferably an hour before breakfast. Children, ½ to 2 tablespoonfuls. Infants, 1 teaspoonful; may be added to the morning feeding.

*Supply:* Magnomint, bottles of 120 ml.

*Note:* Shake well before using. Keep closed; avoid freezing.

## MYCOSTATIN® OINTMENT

**Ointment**

Squibb Nystatin Ointment

Mycostatin is Squibb Nystatin, an antibiotic with antifungal activity against a wide variety of yeasts and yeast-like fungi. Produced by a strain of *Streptomyces noursei*, Mycostatin is the first well tolerated antifungal antibiotic of dependable efficacy for the treatment of cutaneous, oral and intestinal infections caused by *Candida* (Monilia) *albicans*.

Mycostatin is available for topical administration as ointment. Mycostatin Ointment, Squibb Nystatin in Plastobase, is supplied in 10 Gm. tubes providing 100,000 units nystatin per Gm. of Plastobase® (Squibb Plastisized Hydrocarbon Gel) an emollient and protective vehicle.

Mycostatin is well accepted by patients. It does not stain skin or mucous membrane and provides a simple, convenient means of treating cutaneous moniliasis.

*Action:* In concentrations of 2.0 units/ml. or more, Mycostatin is fungistatic *in vitro* against a variety of yeasts and yeast-like fungi, including the principal fungi pathogenic to man. No appreciable activity is exhibited against bacteria.

Mycostatin provides specific therapy for all localized forms of moniliasis. Symptomatic relief is rapid, often occurring within 24 to 72 hours after the initiation of treatment. Cure is effected both clinically and mycologically in most cases of localized moniliasis.

*Advantages:*

* specific therapy
* virtually nontoxic and nonsensitizing
* rapid relief of symptoms
* no development of resistance in clinical practice
* enthusiastic patient acceptance

*Indications:* Mycostatin Ointment is indicated in the treatment of cutaneous mycotic

infections caused by *Candida* (Monilia) *albicans*. If this organism is the primary cause of infection, such dermatologic conditions as "athlete's foot" (dermatophytosis), perleche, paronychia, intertrigo, "diaper rash" and other cutaneous lesions can be expected to respond. Mycostatin Ointment is also indicated in conjunction with Mycostatin Oral Tablets in the local treatment of chronic or resistant vaginal or cutaneous moniliasis, especially when autoreinfection from the intestinal tract is a possibility.

*Administration and Dosage:* Mycostatin Ointment should be applied liberally to affected areas twice daily or as indicated until healing is complete.

*Side Effects:* Mycostatin is virtually nontoxic and nonsensitizing and well tolerated by all age groups including debilitated infants, even on prolonged administration. If irritation on topical application should occur, discontinue medication.

*Supply:* Tubes of 10 Gms.

*Expiration date* 36 months. May be stored at room temperature.

## MYCOSTATIN® ORAL TABLETS

**Tablets**

Squibb Nystatin Tablets

Mycostatin is Squibb Nystatin, an antibiotic with antifungal activity against a wide variety of yeasts and yeast-like fungi. Produced by a strain of *Streptomyces noursei*, Mycostatin is the first well tolerated antifungal antibiotic of dependable efficacy for the treatment of oral, cutaneous and intestinal infections caused by *Candida* (Monilia) *albicans*.

Mycostatin is available for oral administration in coated tablets containing 500,000 units nystatin.

*Action:* Mycostatin has been found to inhibit the growth of yeast-like flora in the intestinal tract. In concentrations of 2.0 units/ml. or more, Mycostatin is fungistatic *in vitro* against a variety of yeast-like fungi, including the principal fungi pathogenic to man. The antibiotic exhibits no appreciable activity against bacteria.

Following oral administration, Mycostatin is absorbed sparingly. No detectable blood levels are obtained when the antibiotic is given in the recommended therapeutic and prophylactic doses, and only traces of Mycostatin are found in the plasma following oral administration of considerably larger doses. Most of the unabsorbed Mycostatin is passed unchanged in the stool.

*Advantages:*

* specific therapy
* virtually nontoxic and nonsensitizing
* rapid relief of symptoms
* no development of resistance in clinical practice
* enthusiastic patient acceptance

*Indications:* Mycostatin for oral use is intended for the prevention and treatment of infections caused by *Candida* (Monilia) *albicans*. Specifically, Mycostatin is indicated for the treatment of intestinal moniliasis, and for protection against monilial superinfection during antimicrobial or corticosteroid therapy.

Mycostatin Oral Tablets are compatible with all commonly employed antimicrobial agents and may be given concomitantly with these agents. Mycostatin Oral Tablets may be administered as a supplement in the local treatment of chronic or resistant oral, vaginal or cutaneous moniliasis. Mycostatin is worthy of trial in generalized (systemic) moniliasis.

*Dosage:* The usual prophylactic and therapeutic dose is 1 tablet (500,000 units) three times daily. This dosage may be increased to 2 tablets (1,000,000 units) three times daily if intestinal fungi are not adequately suppressed. When given concomitantly with an oral antibacterial agent, Mycostatin should be continued at least as long as the antibacterial agent. Treatment should generally be continued for at least 48 hours after clinical cure to prevent relapse.

*Note:* When monilial lesions of the skin and/or nasal, vaginal or rectal mucosae are present in addition to intestinal infections, these should be treated concomitantly with Mycostatin Ointment, applied locally several times daily.

*Side Effects:* Mycostatin is virtually nontoxic and nonsensitizing and well tolerated by all age groups including debilitated infants, even on prolonged administration. Large oral doses have occasionally produced diarrhoea and gastrointestinal distress.

*Supply:* Mycostatin Oral Tablets, sugar-coated tablets of 500,000 units in bottles of 12.

*Expiration date* 24 months.

## MYCOSTATIN® VAGINAL TABLETS — Vaginal Tablets

Squibb Nystatin Vaginal Tablets

Mycostatin is Squibb Nystatin, an antifungal antibiotic with activity against a wide variety of yeasts and yeast-like fungi. Produced by a strain of *Streptomyces noursei*, Mycostatin is the first well tolerated antifungal antibiotic of dependable efficacy for the treatment of vaginal, cutaneous, oral and intestinal infections caused by *Candida* (Monilia) *albicans*.

For the treatment of monilial infections of the vagina, Mycostatin Vaginal Tablets are available as almond-shaped compressed tablets, supplying 100,000 units nystatin dispersed in a lactose base.

*Action:* In concentrations of 2.0 units/ml. or more, Mycostatin is fungistatic *in vitro* against a variety of yeast-like fungi, including the principal fungi pathogenic for man. *In vivo*, Mycostatin acts primarily against *Candida albicans*, this action being fungicidal and fungistatic. Mycostatin exhibits no appreciable activity against bacteria.

*Indications:* Mycostatin Vaginal Tablets are intended for the local treatment of vaginal mycotic infections caused by *Candida* (Monilia) *albicans*. In both pregnant and non-pregnant women, Mycostatin offers an effective and painless control of such troublesome and unpleasant symptoms as itching, inflammation and foul vaginal discharge commonly associated with monilial vaginitis. Mycostatin Vaginal Tablets have proved useful in the control of *Candida albicans* vaginitis prior to delivery in gravid patients. Reports in the literature indicate increasing evidence that the presence of *Candida albicans* in the birth canal at the time of delivery may be one of the major causes of thrush in the newborn.

Local treatment with Mycostatin Vaginal Tablets may be supported by concomitant oral therapy with Mycostatin Oral Tablets, particularly in chronic or recurrent cases when reinfection of the vagina from the intestinal tract is suspected.

*Advantages:* Mycostatin Vaginal Tablets provide specific local therapy for vaginal moniliasis, preserving the normal flora of the vaginal tract. Restoration of normal bacterial flora of the vagina is promoted by the lactose content of the tablets. Symptomatic relief is rapid, often occurring within 24 to 72 hours after initiation of treatment. Cure is effected both clinically and mycologically in most cases of localized moniliasis.

*Administration and Dosage:* Mycostatin Vaginal Tablets are specifically designed for ease of administration. The almond-shaped tablet should be inserted deep into the vagina once or twice daily. The usual dosage of Mycostatin Vaginal Tablets for the treatment of monilial vaginitis in gravid and non-gravid patients is 1 or 2 tablets (100,000 or 200,000 units) intravaginally daily for two weeks, or as required. In most cases two weeks of therapy will be sufficient, but in some cases more prolonged treatment may be necessary. Adjunctive measures such as therapeutic douches are unnecessary and sometimes inadvisable. Cleansing douches may be used by non-pregnant women, if desired, for aesthetic purposes. It is important that therapy be continued during menstruation. In chronic or recurrent cases of monilial vaginitis, when autoreinfection from the intestinal tract is suspected, concomitant therapy with Mycostatin Oral Tablets, 1 tablet (500,000 units) three times daily, is advised.

In gravid patients to prevent thrush in the newborn, a dosage of 1 or 2 Mycostatin Vaginal Tablets daily for three to six weeks before term is suggested.

*Side Effects:* Mycostatin is virtually nontoxic and nonsensitizing and well tolerated by all age groups, even on prolonged administration. If irritation should occur, discontinue medication.

*Supply:* Each tablet containing 100,000 units, bottles of 12.

*Expiration date* 12 months. Keep in a cool place.

## MYSTECLIN® 100-100 Capsules

Squibb Tetracycline Hydrochloride and Nystatin

Mysteclin 100-100 is Squibb Tetracycline Hydrochloride and Nystatin. The preparation is specifically designed to provide children in one capsule a broad spectrum antibiotic, Squibb Tetracycline, and an effective antifungal antibiotic, Mycostatin® (Squibb Nystatin).

Tetracycline is a crystalline antibiotic resembling oxytetracycline and chlortetracycline in chemical configuration and antimicrobial activity. However, tetracycline offers the advantage of higher blood levels and fewer gastrointestinal side effects than its two analogues. The antibiotic is well absorbed and diffuses readily into tissues and body fluids. Nystatin is an antibiotic produced by a strain of *Streptomyces noursei*. It is the first safe, broadly effective antifungal antibiotic which has exhibited excellent fungistatic and fungicidal action against a wide variety of fungi and yeasts. The drug is not appreciably absorbed from the gastrointestinal tract.

Mysteclin 100-100 is available in capsules providing 100 mg. tetracycline hydrochloride and 100,000 units nystatin.

*Rationale for Use:* Oral antibiotic therapy, particularly with broad spectrum antibiotics, may result in certain complications, including gastrointestinal complaints, diarrhoea, lesions affecting the oral cavity (thrush), and anorectal disturbances, which are attributable to an overgrowth of *Candida* (monilia) in the gastrointestinal tract. In rare instances, this may lead to systemic infections which are very difficult to control. Fatal cases of moniliasis following intensive oral antibacterial therapy have been reported. Mycostatin (Squibb Nystatin) has been employed successfully in the prevention and management of intestinal moniliasis, particularly that occurring following the use of orally administered broad spectrum antibiotics. The combined administration of Mycostatin (Squibb Nystatin) and Squibb Tetracycline, as provided by Mysteclin 100-100, affords both antimicrobial therapy with a broad spectrum antibiotic as well as safe and effective prevention of overgrowth of *Candida*. Mysteclin 100-100 is particularly useful in patients receiving prolonged or intensive tetracycline therapy and in individuals with debilitating diseases in whom an overgrowth of *Candida* may lead to fatal infection.

It is also useful in infants (particularly prematures), as well as in any patient concurrently receiving cortisone or related steroid therapy and in subjects who have had a monilial complication on previous broad spectrum antibiotic therapy.

*Indications:* Mysteclin 100-100 is indicated for the many common infections, including those of the respiratory, gastrointestinal and genitourinary systems, which are amenable to tetracycline therapy. Infections caused by gram-positive and gram-negative bacteria, spirochaetes, viruses of the lymphogranuloma-psittacosis-trachoma group, rickettsiae, and *Endamoeba histolytica* can be expected to respond.

Representative infections in which Mysteclin 100-100 may be used are:

*Pneumococcal Infections*
lobar pneumonia

*Streptococcal Infections*
cellulitis
bronchopneumonia
follicular tonsillitis
meningitis
otitis media
pharyngitis
scarlet fever
septic sore throat
tonsillitis
tracheobronchitis
urinary tract infections

*Staphylococcal Infections*
abscesses
acute bronchitis
furunculosis
impetigo
laryngotracheitis
ophthalmic infections
osteomyelitis
otitis media
pharyngitis
septicaemia
sinusitis
tracheobronchitis
urinary tract infections

*Neisseria Infections*
gonorrhoea
meningitis

*Proteus Infections* (due to tetracycline sensitive strains)

*Escherichia coli Infections*
abscesses
peritonitis
urinary tract infections

*Shigella Infections*
bacillary dysentery

*Haemophilus Infections*

*Pertussis*

*Rickettsial Infections*
epidemic typhus
Rocky Mountain spotted fever

*Virus-like Infections*
lymphogranuloma
psittacosis
trachoma

*Intestinal Amoebic Infections*

*Acute Brucellosis*
(in conjunction with streptomycin)

Mysteclin 100-100 is particularly valuable in the treatment of mixed infections and in conditions in which the causal agent has not been specifically identified, for example, pneumonia, peritonitis, chronic bronchiectasis, sinusitis, urinary tract infections, and pancreatitis. Mysteclin 100-100 is also recommended for mixed infections of the eye including conjunctivitis, corneal infections, periorbital infection and some forms of blepharitis, and for such pyogenic dermatologic conditions as secondarily infected atopic dermatitis, sycosis, and eczematous otitis externa. Mysteclin 100-100 is particularly useful in pre-operative and post-operative prophylaxis.

*Administration and Dosage: Infants and Children:* The dosage for infants and children is based on the tetracycline content of Mysteclin 100-100 Capsules so as to supply 20 mg./Kg. of body weight given in divided doses per day. For example, a child weighing 15 Kg. should receive 1 Mysteclin 100-100 Capsule 3 times daily or a total of 300 mg. tetracycline per day. Dosage may be modified according to the type and severity of the infection being treated.

For administration to infants, the contents of a Mysteclin 100-100 Capsule may be

added to soft foods such as jelly or custards. Extemporaneous mixtures thus prepared should be used immediately.

Treatment with Mysteclin 100-100 should be continued for at least 24 to 48 hours after symptoms have subsided and temperature has become normal. Prolonged treatment may be necessary in some instances. Subacute bacterial endocarditis due to susceptible organisms may require one or more courses of therapy each lasting for a period of 6 to 8 weeks, and acute staphylococcal infections several courses each of 10 to 14 days, if necessary.

When Mysteclin 100-100 is used for streptococcal respiratory infections in penicillin-sensitive patients, administration of the drug should be continued for 10 days. It has been found that rheumatic fever can be prevented in most instances if adequate blood concentrations are maintained for 10 days.

*Side Effects:* Since not all gastrointestinal side effects are due to moniliasis, nausea, vomiting and diarrhoea may occur in some patients. However, tetracycline is generally well tolerated, undesirable gastrointestinal side effects occurring significantly less frequently than with its two analogues, oxytetracycline and chlortetracycline. Apart from those side effects arising from monilial infections which are largely eliminated, the incidence and severity of side effects following combined use of tetracycline and nystatin, is no greater than that occurring following the use of tetracycline alone.

*Precaution:* Mysteclin 100-100 therapy should be given under the constant supervision of a physician.

*Supply:* Bottles of 12 capsules.

*Expiration date* 18 months.

## MYSTECLIN-C®

**Capsules**

Squibb Tetracycline Hydrochloride with Ascorbic Acid (Vitamin C) and Amphotericin B (Fungizone®)

Mysteclin-C Capsules contain 250 mg. crystalline tetracycline hydrochloride with 250 mg. vitamin C and 50 mg. amphotericin B (Fungizone). Although the chemical and physical properties as well as the antibacterial spectrum of tetracycline hydrochloride resemble those of oxytetracycline and chlortetracycline, tetracycline hydrochloride offers the advantage of greater stability in plasma and, on oral administration, few gastrointestinal side effects. In addition, tetracycline hydrochloride rapidly achieves effective blood and tissue concentrations.

*Action:* Tetracycline hydrochloride provides proven therapeutic effectiveness against infections caused by a broad spectrum of micro-organisms including both gram-positive and gram-negative bacteria, spirochaetes, certain rickettsiae, viruses of the lymphogranuloma-psittacosis-trachoma group, and *Endamoeba histolytica.* Following oral administration tetracycline hydrochloride is readily absorbed from the gastrointestinal tract with prompt establishment of fully effective blood concentrations. The antibiotic is rapidly diffused into various body fluids, including

the cerebrospinal, peritoneal and pleural fluids, and the saliva. It appears to be mainly excreted in the urine, although some portions of the ingested drug are excreted unchanged in the faeces.

Vitamin C is known to disappear from the blood of patients with fever more quickly than it does from the normal persons. The accelerated metabolism associated with the elevated temperature is considered to be the cause of the increased utilization of this vitamin. This is particularly significant in the human beings, who cannot synthesize this vitamin in the body. Vitamin C is known to play the following roles in infection:

1. It assists in resistance of infection
2. It helps in the production of antibodies
3. It has a stimulative influence on phagocytic activity
4. It is necessary for many detoxification mechanisms

Vitamin C is also helpful in wound healing. Vitamin C as contained in the formulation provides an adequate supply to counterbalance the depletion of vitamin C in infected and febrile states.

Mysteclin-C also contains prophylactic amounts of amphotericin B (Fungizone) for specific protection against monilial overgrowth in the gastrointestinal tract. Monilial overgrowth may occur in some patients taking broad spectrum antibiotics—particularly elderly or debilitated patients; patients on high or prolonged antibiotic dosage; diabetics; infants, especially prematures; patients on corticoid therapy; patients who have developed moniliasis on previous broad spectrum therapy; and women, particularly during pregnancy. These patients especially are potential candidates for therapy with Mysteclin-C Capsules whenever tetracycline antibiotics are indicated.

*Indications:* Mysteclin-C Capsules are indicated for the many common infections including those of the respiratory, gastrointestinal and genitourinary systems which are amenable to tetracycline therapy.

Representative infections in which Mysteclin-C Capsules may be used are:

*Pneumococcal Infections*
lobar pneumonia

*Streptococcal Infections*
cellulitis
broncho pneumonia
follicular tonsillitis
meningitis
otitis media
pharyngitis
scarlet fever
septic sore throat
tonsillitis
tracheobronchitis
urinary tract infections

*Staphylococcal Infections*
abscesses
acute bronchitis
furunculosis
impetigo
laryngotracheitis
ophthalmic infections
osteomyelitis
otitis media
pharyngitis
septicaemia
sinusitis
tracheobronchitis
urinary tract infections

*Neisseria Infections*
gonorrhoea
meningitis

*Proteus Infections* (due to tetracycline sensitive strains)

*Escherichia coli Infections*
abscesses
peritonitis
urinary tract infections

*Shigella Infections*
bacillary dysentery

*Haemophilus Infectons*

*Pertussis*

*Rickettsial Infections*
epidemic typhus
Rocky Mountain spotted fever

*Virus-like Infections*
lymphogranuloma
psittacosis
trachoma

*Intestinal Amoebic Infections*

*Acute Brucellosis*
(in conjunction with streptomycin)

Mysteclin-C Capsules are particularly valuable in the treatment of mixed infections due to susceptible organisms and in conditions in which the causal agent has not been specifically identified, for example, pneumonia, peritonitis, chronic bronchiectasis, sinusitis, urinary tract infections, postpartum endometritis, puerperal mastitis, and pancreatitis. The capsules are also recommended for mixed infections of the eye including conjunctivitis, corneal infection, periorbital infection, uveitis and some forms of blepharitis and for such pyogenic dermatologic conditions as secondarily infected atopic dermatitis, sycosis and eczematous otitis externa. The capsules are also useful in pre-operative and post-operative prophylaxis.

*Dosage:* Dosage should be based on the tetracycline content. The suggested *minimum* adult dosage is 250 mg. four times daily. Higher dosages, such as 500 mg. four times daily, may be required for severe infections or for those infections which do not respond to the smaller dose. In general, the paediatric dosage should supply 20 to 40 mg. tetracycline per Kg. of body weight each day, in divided doses, depending on the type and severity of the infection.

Treatment of most common infections should generally continue for 24 to 48 hours after symptoms and fever subside. However, if the capsules are used in the treatment of streptococcal infections, therapy should be continued for a full 10 days to guard against the risk of rheumatic fever or glomerulonephritis. Even more prolonged therapy is necessary for subacute bacterial endocarditis and may be required in certain staphylococcal infections.

*Side Effects:* Tetracycline hydrochloride is generally well tolerated. Undesirable side effects such as nausea, vomiting and diarrhoea are significantly less frequent with tetracycline hydrochloride than with the two analogues, oxytetracycline and chlortetracycline. If necessary, the capsule may be given with cold milk or a light meal.

*Precautions:* As with any antibiotic preparation, prolonged use may result in overgrowth of non-susceptible organisms. Constant observation of the patient is essential. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted.

Tetracycline may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans. However, use of tetracycline during tooth development (i.e., last trimester of pregnancy, neonatal period and early childhood) may cause discoloration of the teeth (i.e., yellow-grey-brownish). This effect occurs mostly during long-term use of the drug but it has also been observed in usual short-treatment courses.

*Warning:* If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulation of the drug and possible liver toxicity. Under such conditions, lower than usual doses are indicated and if therapy is prolonged, tetracycline serum level determinations may be advisable.

*Supply:* Nested packing of 100.

*Expiration date* 24 months.

## MYSTECLIN-V® IMPROVED PEDIATRIC DROPS — Liquid

Squibb Tetracycline Buffered with Potassium Metaphosphate and Amphotericin B (Fungizone®)

Mysteclin-V Improved Pediatric Drops provide in a form particularly well suited for paediatric use. Each ml. of Mysteclin-V Improved Pediatric Drops contains tetracycline equivalent to 100 mg. tetracycline hydrochloride, buffered with potassium metaphosphate, and 20 mg. amphotericin B, in a fruit-flavoured aqueous preparation. The preparation also contains 0.2% sodium benzoate and 0.15% sodium metabisulphite as preservatives.

Mysteclin-V Improved Pediatric Drops are supplied with a dropper which dispenses 5 mg. tetracycline and 1 mg. amphotericin B per drop (25 mg. tetracycline and 5 mg. amphotericin B in 5 drops).

*Action:* Mysteclin-V Improved has been designed to provide simultaneous antimicrobial therapy and antimonilial prophylaxis, a concept first developed by Squibb.

Mysteclin-V Improved contains the broad spectrum antibiotic, tetracycline, well-known for its pronounced antimicrobial effect against a wide range of pathogenic organisms. Mysteclin-V Improved produces exceptionally high initial tetracycline blood levels as well as excellent diffusion to tissues and body fluids.

Furthermore, Mysteclin-V Improved also contains prophylactic amounts of the new antifungal antibiotic, Fungizone (Squibb Amphotericin B). This antibiotic, first isolated and described by the Squibb Institute for Medical Research, is substantially more active *in vitro* against *Candida* strains than nystatin. It has been widely used by the intravenous route in the successful treatment of many deep-seated mycotic infections.

Given orally, Fungizone is extremely well tolerated and is virtually non-toxic in prophylactic doses. Since it is poorly absorbed from the gastrointestinal tract after oral administration, Fungizone exerts a high degree of activity against *Can-*

*dida* species in the intestinal tract and prevents the overgrowth of these organisms commonly associated with broad spectrum antibiotic therapy. (Fungizone has no antibacterial activity.) By suppressing overgrowth of *Candida* in the gastrointestinal tract, thereby minimizing a possible reservoir of this organism, Mysteclin-V Improved provides added protection for the patient against potentially troublesome, or even serious, monilial superinfections, e.g., intestinal, anogenital, mucocutaneous moniliasis.

*Indications:* Mysteclin-V Improved is indicated for the many common infections, including those of the respiratory, gastrointestinal, and genitourinary systems, which are amenable to tetracycline therapy. Infections caused by gram-positive and gram-negative bacteria, spirochaetes, viruses of the lymphogranuloma-psittacosis-trachoma group, rickettsiae, and *Endamoeba histolytica* can be expected to respond. Because of its wide range of antimicrobial activity, Mysteclin-V Improved is particularly useful in the treatment of mixed infections due to susceptible organisms. Monilial overgrowth may occur in patients taking broad spectrum antibiotics. Although it is impossible to predict exactly which paediatric patient will develop monilial complications and which will not, certain types of patients are known to be particularly susceptible to moniliasis. Among these are infants, particularly prematures; debilitated patients, such as in kwashiorkor; patients on high or prolonged antibiotic dosage; diabetics; patients on corticoid therapy; patients who have developed moniliasis on previous broad spectrum therapy. Because the danger of monilial complications is greatest in these patients, they are candidates for therapy with Mysteclin-V Improved.

*Dosage:* Mysteclin-V Improved dosage should be based on its tetracycline content. In general, the paediatric dosage should supply 20 to 40 mg. tetracycline per Kg. of body weight each day, in divided doses, depending on the type and severity of the infection. The following paediatric dosages are representative:

Below 5 Kg. : 25 mg. tetracycline ( 5 drops) four times daily
5 to 10 Kg. : 50 mg. tetracycline (10 drops) four times daily
10 to 15 Kg. : 75 mg. tetracycline (15 drops) four times daily
15 to 20 Kg. : 100 mg. tetracycline (20 drops) four times daily

Treatment of most common infections should continue for 24 to 48 hours after symptoms and fever subside. However, if Mysteclin-V Improved is used in the treatment of streptococcal infections, therapy should be continued for a full 10 days to guard against the risk of rheumatic fever, higher dosage and even more prolonged therapy would be necessary for subacute bacterial endocarditis and might be required for certain staphylococcal infections.

*Precautions:* With the use of any broad spectrum antibiotic, the patient should be carefully watched for signs of secondary infection caused by nonsusceptible organisms. If such infections appear, Mysteclin-V Improved should be discontinued and/or other appropriate measures taken.

*Side Effects:* Since not all gastrointestinal side effects are due to moniliasis, nausea, vomiting, and diarrhoea may occur in some patients. However, tetracycline is generally well tolerated, undesirable gastrointestinal side effects occurring

significantly less frequently than with the two analogues, oxytetracycline and chlortetracycline.

*Warning:* If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulation of the drug and possible liver toxicity. Under such conditions, lower than usual doses are indicated and if therapy is prolonged, tetracycline serum level determinations may be advisable.

*Supply:* Bottles of 10 ml. with dropper.

*Expiration date* 18 months.

## MYSTECLIN-V® IMPROVED SYRUP

**Syrup**

Squibb Tetracycline Buffered with Potassium Metaphosphate and Amphotericin B (Fungizone®)

Mysteclin-V Improved Syrup provides Squibb Tetracycline and Amphotericin B (Fungizone) in a form particularly well suited for children. Each 5 ml. of Mysteclin-V Improved Syrup contains tetracycline equivalent to 125 mg. tetracycline hydrochloride, buffered with potassium metaphosphate and 25 mg. amphotericin B in a pleasantly flavoured syrup.

A 5 ml. spoon measure is supplied with each Mysteclin-V Improved Syrup.

*Action:* Mysteclin-V Improved Syrup has been designed to provide simultaneous antimicrobial therapy and antimonilial prophylaxis, a concept first developed by Squibb.

Mysteclin-V Improved Syrup contains the broad spectrum antibiotic, tetracycline, well known for its pronounced antimicrobial effect against a wide range of pathogenic organisms. Mysteclin-V Improved Syrup produces high initial tetracycline blood levels as well as excellent diffusion to tissues and body fluids.

Furthermore, Mysteclin-V Improved Syrup also contains prophylactic amounts of the new antifungal antibiotic, Fungizone (Squibb Amphotericin B). This antibiotic, first isolated and described by the Squibb Institute for Medical Research, is substantially more active *in vitro* against *Candida* strains than nystatin. It has been widely used by the intravenous route in the successful treatment of many deep-seated mycotic infections.

Given orally, Fungizone is extremely well tolerated and is virtually non-toxic in prophylactic doses. Since it is poorly absorbed from the gastrointestinal tract after oral administration, Fungizone exerts a high degree of activity against *Candida* species in the intestinal tract and prevents the overgrowth of these organisms commonly associated with broad spectrum antibiotic therapy. (Fungizone has no antibacterial activity.) By suppressing overgrowth of *Candida* in the gastrointestinal tract, thereby minimizing a possible reservoir of this organism, Mysteclin-V Improved Syrup provides added protection for the patient against potentially troublesome, or even serious, monilial superinfections, e.g., intestinal, anogenital, mucocutaneous moniliasis.

*Indications:* Mysteclin-V Improved Syrup is indicated for the many common infections, including those of the respiratory, gastrointestinal, and genitourinary systems, which are amenable to tetracycline therapy. Infections caused by gram-positive and gram-negative bacteria, spirochaetes, viruses of the lymphogranuloma-psittacosis-trachoma groups, rickettsiae, and *Endamoeba histolytica* can be expected to respond. Because of its wide range of antimicrobial activity, Mysteclin-V Improved Syrup is particularly useful in the treatment of mixed infections due to susceptible organisms.

Monilial overgrowth may occur in patients taking broad spectrum antibiotics. Although it is impossible to predict exactly which patient will develop monilial complications and which will not, certain types of patients are known to be particularly susceptible to moniliasis. Among these are infants, particularly prematures; debilitated patients; patients on high or prolonged antibiotic dosage; diabetics; patients on corticoid therapy; patients who have developed moniliasis on previous broad spectrum therapy. Because the danger of monilial complications is greatest in these patients, they are candidates for therapy with Mysteclin-V Improved Syrup.

*Dosage:* The dosage of Mysteclin-V Improved Syrup should be based on its tetracycline content. In general the paediatric dosage should supply 20–40 mg. tetracycline per Kg. of body weight per day in divided doses, depending upon the severity of infection. The following dosage schedule will usually be found to be adequate.

| *Body weight* | | *Dose* |
|---|---|---|
| 9 Kg. (20 lbs. approx.) | = | ½ teaspoonful q.i.d. |
| 18 Kg. (40 lbs. approx.) | = | 1 teaspoonful q.i.d. |
| 27 Kg. (60 lbs. approx.) | = | 1½ teaspoonfuls q.i.d. |
| 36 Kg. (80 lbs. approx.) | = | 2 teaspoonfuls q.i.d. |

It is recommended that treatment with Mysteclin-V Improved Syrup should continue for one to two days after symptoms and fever subside. However, for streptococcal infections, therapy with Mysteclin-V Improved Syrup should be continued for 10 more days after the fever has subsided to guard against the risk of rheumatic fever; higher dosage and even more prolonged therapy would be necessary for subacute bacterial endocarditis and might be required for certain staphylococcal infections.

*Precautions:* With the use of any broad spectrum antibiotic, the patient should be carefully watched for signs of secondary infection caused by nonsusceptible organisms. If such infections appear, Mysteclin-V Improved Syrup should be discontinued and/or other appropriate measures taken.

*Side Effects:* Since not all gastrointestinal side effects are due to moniliasis, nausea, vomiting, and diarrhoea may occur in some patients. However, tetracycline is generally well tolerated, undesirable gastrointestinal side effects occurring significantly less frequently than with the other analogues of tetracycline.

*Warning:* If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulation of the drug and possible liver toxicity.

Under such conditions, lower than usual doses are indicated and if therapy is prolonged, tetracycline serum level determinations may be advisable.

*Supply:* Bottles of 60 ml. with a 5 ml. spoon measure.

*Note:* Keep tightly closed in a cool place, protected from light.

*Expiration date* 18 months.

## NAVITOL® MALT COMPOUND — Syrup

Squibb Syrup of Vitamins with Iron

Navitol Malt Compound is an agreeable vitamin-iron dietary supplement, especially for children. One tablespoonful (½ fluid ounce or 20 grammes), the suggested daily dose of Navitol Malt Compound supplies:

| | |
|---|---|
| Vitamin A | 5,000 I.U. |
| Vitamin D | 1,000 I.U. |
| Vitamin $B_1$ (Thiamine Hydrochloride) | 1 mg. |
| Vitamin $B_2$ (Riboflavine) | 1.5 mg. |
| Niacinamide | 10 mg. |
| Iron, as ferrous sulphate | 10 mg. |

and is composed of 63.0 per cent carbohydrate, 1.4 per cent fat, 5.3 per cent protein, 1.5 per cent ash and 61 calories per ½ fluid ounce (1 tablespoonful).

*Advantages:* Navitol Malt Compound is a thick, dark brown, prune-like flavoured syrup that is ideal for children. Their co-operation is encouraged by this agreeable preparation. One tablespoonful of Navitol Malt Compound supplies the full recommended dietary allowances of the three important B Complex vitamins and Iron for children seven to nine years of age (the median age group). It also supplies a dosage of vitamins A and D which is the recognized optimum in paediatric practice.

*Dosage:* One tablespoonful daily, or more as directed by the physician.

*Supply:* Bottles of 225 Gms. and 450 Gms.

*Note:* Keep in a cool place in order to avoid vitamin $B_1$ loss.

*Expiration date* 18 months.

## NYDRAZID® — Tablets, Sterile Solution

Squibb Isoniazid

Nydrazid is Squibb Isoniazid, a potent antituberculous drug. It is available as tablets providing 50, 100 and 300 mg. isoniazid. For intramuscular use, Nydrazid is available in vials of 10 ml., each ml. providing 100 mg. isoniazid. Intramuscular administration of Nydrazid is intended for use whenever the oral route of administration is not possible. Nydrazid Injection may also be employed topically for tuberculous empyema or effusion. The intramuscular preparation

may crystallize at low temperatures and should be warmed to room temperature to insure solution before use.

*Advantages:* Following administration, Nydrazid is distributed throughout the body tissues and fluids. The drug penetrates readily into necrotic tuberculous tissue and is effective against intracellular organisms.

*Indications:* Nydrazid is recommended in the treatment of tuberculosis, preferably in conjunction with other antituberculous drugs. Nydrazid, like any other antituberculous drugs, must be considered an adjuvant in the careful long-range management of tuberculosis. As is true of other antituberculous drugs, the chief short-coming of isoniazid lies in the emergence of resistant organisms, suggesting combined use of isoniazid with other antituberculous agents. Clinical experience has shown that, due to synergism, concomitant administration of isoniazid with streptomycin and/or para-amino-salicylic acid (PAS) may provide an increased antituberculous effect and tends to prevent or delay development of resistant organisms. Nydrazid in conjunction with both PAS and streptomycin should be reserved for treatment of the more serious forms of tuberculosis (renal, miliary and meningeal). Nydrazid has proved useful in the treatment of Hansen's disease (Leprosy), favourable results having been observed particularly in patients with the lepromatous type of the disease.

Nydrazid is also recommended for oral prophylactic use in all infants and children under 3 years of age who exhibit positive reactions to either the Mantoux or the tuberculin patch test, and to all children who have recently converted from a negative to positive tuberculin reaction.

*Precautions:* In patients with epilepsy, isoniazid should be administered cautiously and only when the epileptic condition has been controlled with appropriate medication. Isoniazid should be given with caution and in the lowest effective doses where renal damage is suspected or known to exist. The drug should not be used in the treatment of renal tuberculosis unless adequate facilities for the estimation of isoniazid blood levels are available. Detection of isoniazid levels is readily accomplished by chemical analysis.

*Side Effects:* Undesirable side effects are generally minimal with therapeutic doses of isoniazid. Untoward effects are limited to central nervous system stimulation, including hyper-reflexia, paraesthesias, vertigo, drowsiness, excitement, euphoria, delay in micturition, muscular twitching, dryness of the mouth, and peripheral neuritis. These reactions are more likely to occur in elderly patients than in young children and adolescents. Concomitant administration of pyridoxine with isoniazid is used to prevent or control peripheral neuritis. If signs of marked central nervous system stimulation are encountered, isoniazid therapy should be interrupted.

*Administration and Dosage:* CLINICAL APPLICATION– The recommended dosage for isoniazid in the treatment of tuberculous or Hansen's disease is 3 to 5 mg./Kg. of body weight per day, either in a single dose or in divided doses. In serious cases of tuberculosis such as miliary or meningeal tuberculosis, the recommended daily dosage for isoniazid is 7 mg./Kg. for seven days and thereafter 3 mg./Kg. Oral dosage should be given with meals.

Usually for an adult patient one 100 mg. tablet is given three times a day; however, for convenience of once-a-day dosage one 300 mg. tablet can be recommended every day.

For oral prophylaxis or for oral or parenteral therapy in infants and children who are rapid inactivators of isoniazid, the recommended daily dosage is 10 to 20 mg./Kg. of body weight (maximum dosage 500 mg. daily) divided into two equal doses, i.e., 5 to 10 mg./Kg. b.i.d.

TREATMENT PROGRAMMES: Clinical experience has shown the following to be acceptable treatment possibilities.

1. *Nydrazid (isoniazid) and para-amino-salicylic acid (PAS).* Suggested dosage regime: A total daily dose of 3 to 5 mg. isoniazid/Kg. for adults and 10 to 20 mg./Kg. for children, with 12 to 16 Gm. PAS, in divided doses per day.

2. *Nydrazid (isoniazid) with streptomycin.* Suggested dosage regime: With a daily dose of 3 to 5 mg. isoniazid/Kg. for adults and 10 to 20 mg./Kg. for children, intramuscular streptomycin is given either: *Daily:* 1 to 3 Gm. for adults with severe constitutional reactions and particularly with extensive pneumonia, miliary or meningeal tuberculosis. (In the latter cases, the suggested daily dose of isoniazid is 7 mg./Kg. for seven days, then 3 mg./Kg.). *Intermittently:* 1 to 3 Gm. twice weekly or every three days for adults without severe constitutional reactions or following adequate response to daily administration. For children, the recommended dosage for streptomycin is 20 mg./Kg.

3. *Nydrazid (isoniazid) with streptomycin and para-amino-salicylic acid (PAS).* This combination should be used only for the more serious forms (renal, miliary, meningeal). The same dosage schedules as given above apply for streptomycin and PAS. For isoniazid, the recommended adult dosage is 7 mg./Kg. for seven days and thereafter 3 mg./Kg.; for children, 10 to 20 mg./Kg. daily.

4. *Nydrazid (isoniazid) alone.* Isoniazid may be used alone in patients unable to tolerate other antituberculous agents. However, the emergence of drug-resistant organisms is likely to occur. Suggested dosage regime: 3 to 5 mg. isoniazid/Kg. for adults and 10 to 20 mg./Kg. for children, divided and given in two equal doses per day.

*Supply:* Tablets: 50 mg., bottles of 1000. 100 mg., bottles of 100 and 1000; and tins of 2500. 300 mg., bottles of 250. Injection: 100 mg. per ml., 10 ml. vials.

*Expiration date* 18 months for Nydrazid Injection.

## NYZET®

**Tablets**

## NYZET® FORTE

**Tablets**

Squibb Isoniazid (Nydrazid®) - Thiacetazone

Nyzet and Nyzet Forte are Squibb Isoniazid-Thiacetazone combinations for antituberculous therapy. Nydrazid, Squibb Isoniazid, and thiacetazone are individually potent antituberculous drugs. As is true of other antituberculous agents,

the chief shortcoming of isoniazid and thiacetazone when given alone lies in the emergence of resistant organisms. Clinical experience has shown that combination of isoniazid with thiacetazone can provide an increased antituberculous effect and tends to prevent or delay development of resistant organisms. This combination has proved to be an ideal choice as the second line of treatment. It can be used even as the first line of treatment in patients unable to tolerate the streptomycin drugs. Nyzet and Nyzet Forte can be given in combination with streptomycin therapy also. Each Nyzet Tablet provides 75 mg. of isoniazid and 37.5 mg. of thiacetazone, while each Nyzet Forte Tablet provides 300 mg. of isoniazid and 150 mg. of thiacetazone.

*Administration and Dosage:* Nyzet and Nyzet Forte Tablets are administered orally. The most effective dosage is 300 mg. of isoniazid combined with 150 mg. of thiacetazone. (The dosage is to be based on the isoniazid content, the recommended dosage for isoniazid being 3 to 5 mg./Kg. body weight.) Thus the usual adult dose will be one Nyzet Tablet four times a day, as divided doses or one Nyzet Forte Tablet a day, as a single dose. Oral dosages should be given preferably with meals. The duration of the therapy and concomitant use of other antituberculous agents will have to be decided by the physician and will depend on the clinical, bacteriological and radiological follow-up.

*Side Effects:* Undesirable side effects are generally minimal with therapeutic doses of Nyzet and Nyzet Forte. Untoward effects are limited to central nervous system stimulation, including hyper-reflexia, paraesthesias, vertigo, drowsiness, excitement, euphoria, delay in micturition, muscular twitching, dryness of mouth and peripheral neuritis. Liver damage, anaemia, agranulocytosis and proteinurea are also occasionally described. It is advisable for patients on Nyzet therapy to have periodical examination of urine and blood picture. Skin hypersensitivity reactions are also reported. Early administration of antihistamines can be of help. If the reaction is severe, the drug should be discontinued.

*Precautions:* The drug should be used with caution in patients with epilepsy, renal damage or liver damage.

*Supply:* Nyzet—Nested packing of 1000 (10 bottles of 100's).
Nyzet Forte—Bottles of 30, and nested packing of 1000 (10 bottles of 100's).

## OXYSTECLIN®

**Parenteral Solution**

Squibb Oxytetracycline Intramuscular

Oxysteclin (Squibb Oxytetracycline Intramuscular) is a ready solution providing 50 mg. and 125 mg. Oxytetracycline per ml. along with 2% lidocaine, as anaesthetic agent, in multi-dose vials and single-dose ampoules.

*Action:* Oxysteclin (Squibb Oxytetracycline Intramuscular) is a potent antimicrobial agent. It rapidly attains fully effective blood and tissue levels. It is excreted through bile and urine in biologically active form. In general, tetracyclines are primarily used for the treatment of gram-negative bacillary infections, rickettsial diseases, gram-positive infections amenable to oxytetracycline. It is also effective in Miyagawanella, i.e., large viruses of the lymphogranuloma-psittacosis-trachoma group.

*Indications:* Oxysteclin (Squibb Oxytetracycline Intramuscular) exhibits antimicrobial activity against a wide variety of gram-negative and gram-positive bacteria, rickettsiae, spirochaetes, *Endamoeba histolytica* and Miyagawanella ("large viruses" of the lymphogranuloma-psittacosis-trachoma group).

This preparation is particularly valuable in the treatment of mixed infections and in conditions in which the causal agent has not been specifically identified. The preparation is also recommended for the mixed infections of eye, and for such pyogenic dermatologic conditions as secondarily infected atopic dermatitis, sycosis, and eczematous otitis externa.

Intramuscular oxytetracycline therapy is intended for those patients who are unable or unwilling to take oral therapy.

*Note:* A number of strains of *Staphylococci* and *Streptococci* have shown resistance to tetracyclines. A few strains of *Pneumococci*, *E. coli* and *Shigellae* also have been reported as resistant. Indicated laboratory studies, including sensitivity tests, should be performed.

*Contraindications:* This drug is contraindicated in individuals with a history of hypersensitivity to oxytetracycline or lidocaine.

*Warning:* If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulation of the drug and possible liver toxicity. Under such conditions, lower than usual doses are indicated and if therapy is prolonged, oxytetracycline serum level determination may be advisable.

Certain hypersensitive individuals may develop a photodynamic reaction precipitated by a direct exposure to natural or artificial sunlight during the use of this drug. This reaction is usually of the photoallergic type which may also be produced by other tetracycline derivatives. Individuals with a history of photosensitivity reactions should be instructed to avoid direct exposure to natural or artificial sunlight while under treatment with this or other tetracycline drugs, and treatment should be discontinued at first evidence of skin discomfort.

*Note:* Photosensitization reactions have occurred most frequently with dimethylchlor tetracycline, and very rarely with oxytetracycline and tetracycline.

*Precautions:* Since sensitivity reactions are more likely to occur in persons with a history of allergy, asthma, hay fever, or urticaria, the preparation should be used with caution in such individuals. Cross-sensitization among the various tetracyclines is extremely common.

As with any preparation for intramuscular injection, care should be taken to insure intramuscular delivery (see *Administration and Dosage*).

During long-term therapy, periodic assessment of organ system function, including renal, hepatic and haematopoietic systems, should be made.

As with any antibiotic preparation, prolonged use may result in overgrowth of non-susceptible organisms. Constant observation of the patient is essential. Should superinfection occur, the preparation should be discontinued and/or appropriate therapy instituted.

*Note:* Superinfection of the bowel by staphylococci may be life-threatening.

Oxytetracycline may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans. However, use of oxytetracycline during tooth development (i.e., latter half of gestation, neonatal period and early childhood) may cause discoloration of the teeth (i.e., yellow-grey-brownish). This effect occurs mostly during long-term use of the drug but it has also been observed in usual short-treatment courses.

*Adverse Reactions:* Tetracycline in general may produce gastrointestinal irritation (anorexia, epigastric distress, nausea, vomiting) as well as bulky loose stools and diarrhoea. Glossitis, stomatitis, enterocolitis, proctitis and pruritus ani may occur in some patients. Black hairy tongue, sore throat, dysphagia, and hoarseness have been reported. The gastrointestinal side effects are less frequent after parenteral use than after oral administration.

Maculopapular and erythematous skin rashes may occur. A rare case of exfoliative dermatitis has been reported. Photosensitivity, manifested by an exaggerated sunburn reaction, has been observed in some individuals (see *Warning*). Onycholysis and discoloration of the nails have been reported rarely.

Rise in BUN (Blood Urea Nitrogen) has been reported and is apparently dose-related. Urinary loss of nitrogen has been observed in some patients receiving tetracyclines and may result in negative nitrogen balance. Increased excretion of sodium has also been reported. The development of peptic ulcers and bleeding has been observed in uremic patients receiving tetracyclines.

Hypersensitivity reactions may include urticaria, serum sickness-like reactions (fever, rash, arthralgia), angioneurotic oedema, and anaphylactoid shock. If allergic reactions occur, or if an individual idiosyncrasy appears, oxytetracycline therapy should be discontinued.

The use of oxytetracycline during the mineralization phase of tooth development (latter half of gestation, neonatal period, and early childhood) may cause discoloration of the teeth (yellow-grey-brownish) which may sometimes be accompanied by enamel hypoplasia (see *Precautions*).

Anaemia, thrombocytopenic purpura, neutropenia, and eosinophilia have been reported. Tetracyclines may delay blood coagulation.

Hepatic cholestasis has been reported rarely, and is usually associated with high dosage levels.

*Administration and Dosage: Adults:* Intramuscular administration of 200 to 300 mg. per day, given in divided doses of 100 mg. every 8 to 12 hours or as a single daily dose of 250 mg., is generally adequate for the treatment of susceptible infections of mild or moderate severity. In more severe infections or in those patients not responding to the above dosage schedule, 250 mg. every 12 hours may be necessary.

*Infants and Children:* Dosage for infants and children should be proportionately less than the adult dose, depending on the age and weight and on the severity of the condition being treated.

*Note:* Therapy should be continued 1 or 2 days after signs and symptoms of the disease being treated have subsided. However, if an oxytetracycline preparation is used to treat haemolytic streptococcal infections, therapy should be continued for at least 10 days to guard against the risk of rheumatic fever or glomerulonephritis. Even more prolonged therapy is necessary for subacute bacterial endocarditis and may be required in certain staphylococcal infections.

When using Oxysteclin (Squibb Oxytetracycline Intramuscular) in the treatment of brucellosis, the course of therapy should be three weeks and supplemented with intramuscular injections of streptomycin in a dosage of 1 Gm. twice daily the first week, and 1 Gm. daily the second and third weeks in adults. In children, the dosage should be adjusted according to the age and weight of the patient.

*Supply:* Oxysteclin is available in the following packings:
Ampoules: 2 ml. ( 50 mg./ml. and 125 mg./ml. )
Vials: 10 ml. ( 50 mg./ml. )

*Note:* Store in a cool place, protected from light.

*Expiration date* 24 months.

## PENICILLIN G PROCAINE, CRYSTALLINE, IN OIL, SQUIBB (with Aluminium Monostearate)

**Parenteral Suspension**

Each ml. Procaine Penicillin G in Oil, Squibb provides 300,000 units crystalline micronized procaine penicillin G suspended in sesame oil with 2% aluminium monostearate. It is supplied in vials of 10 ml.

*Action:* Because of its low water-solubility, procaine penicillin is slowly absorbed by the tissues. With the addition of aluminium monostearate, absorption takes place even more slowly and more uniformly. Procaine penicillin in oil with 2% aluminium monostearate produces persistent blood levels for at least 24 hours after administration of 300,000 u. The prolonged blood concentrations are shortened with ambulatory patients.

Prolonged penicillin blood levels do not necessarily mean that the drug is present in therapeutically effective amounts, and the dosage suggested in this monograph may, therefore, need to be adjusted accordingly.

*Indications:* The principal field of usefulness of procaine penicillin in oil with aluminium monostearate is the treatment for conditions caused by organisms with a low penicillin resistance—0.1 u. or less penicillin/ml. serum—particularly those organisms requiring prolonged exposure to the drug.

*Contraindications:* This preparation is contraindicated in patients with a history of sensitivity to either procaine or penicillin.

*Precautions:* As with any antibiotic preparation, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. Constant observation of the patient is essential. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted.

Where procaine sensitivity is suspected, perform a preliminary intradermal skin test. If the test is positive, do not administer procaine penicillin.

*Adverse Reactions:* Toxic reactions due to penicillin have been largely limited to sensitivity phenomena. Such reactions may include urticaria, serum sickness-like reactions (fever, rash, arthralgia), other skin rashes and, rarely, anaphylactoid shock. They are more likely to occur in individuals with a history of allergy, asthma, hay fever, or urticaria, and in those who have previously demonstrated hypersensitivity to penicillin. Urticarial, serum sickness-like and other skin rash reactions may be controlled by antihistamines and, if necessary, corticosteroids. Whenever such reactions occur, penicillin should be discontinued unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy. Serious anaphylactoid reactions are not controlled by antihistamines, and require such measures as the immediate use of epinephrine, oxygen, and intravenous corticosteroids.

*Administration:* Squibb Procaine Penicillin G Suspension is administered by deep intramuscular injection, changing the site for each injection; the preferred site is the upper outer quadrant of the buttock. High dosages should be distributed over several injection sites.

1. Use a 20-gauge needle.
2. Shake the vial vigorously to form a uniform suspension.
3. Inject air into the vial for easier withdrawal.
4. After withdrawing dose into the syringe, make sure needle is empty by pulling back the plunger until a small air bubble appears.
5. Insert needle and aspirate to be sure needle is not in a vein.
6. Inject dose slowly. Do not massage the injection site.
7. Wash needle and syringe in warm water and soap immediately.

*Dosage:* The recommended daily dosage of Squibb Procaine Penicillin G Suspension for most penicillin-susceptible infections (except venereal disease) is 300,000 u. and at least 150,000 u. for small children. In severe infections, 300,000 u. every 12 hours is suggested. Streptococcal infections should be treated for 10 days in order to guard against the risk of rheumatic fever or glomerulonephritis. In syphilis, the following dosages are suggested:

*Primary or Secondary Syphilis and Latent Syphilis with Negative Spinal Fluid.* A total of 4,800,000 u. with 2,400,000 u. administered at the first session (1,200,000 u. in each buttock) followed by two injections of 1,200,000 u. each at two- to three-day intervals.

*Latent Syphilis with no Spinal Fluid Examination.* Dosage is the same as for asymptomatic neurosyphilis (see following paragraph).

*Late Syphilis (including symptomatic and asymptomatic neurosyphilis, cardio-vascular, osseous, cutaneous and visceral).* A total of 6,000,000 to 9,000,000 u. administered 1,200,000 u. at three-day intervals. Any benefit from more than 10,000,000 u. has not been demonstrated.

*Early Congenital Syphilis (children under 2 years of age).* Dosage is adjusted to age and body weight. A total of 100,000 u. per Kg. should be given in divided doses at two- to three-day intervals.

*Late Congenital Syphilis.* Treatment is the same as for corresponding stages of acquired syphilis. However, in children under 12, dosage should be adjusted to age and body weight. Interstitial keratitis usually does *not* respond to penicillin. The addition of corticosteroids, applied locally to the eyes, is recommended.

*Syphilis in Pregnancy.* Treatment should correspond to the stage of the disease.

Complications such as cardiovascular syphilis in circulatory failure will require specific measure in addition to penicillin. As a minimum dose, 6,000,000 to 10,000,000 u. is recommended to maintain an adequate blood level for about 8 days. This dose may be supplemented by additional penicillin or other therapeutic measures as indicated.

All cases of penicillin-treated syphilis should receive clinical and serological examinations every six months for at least two or three years.

In gonorrhoea, the following dosage schedules are suggested:

*Uncomplicated Gonorrhoea in Males.* 1,200,000 u. in one intramuscular injection. If discharge persists for three days or more after initial treatment, and smear or culture remains positive, re-treat with a single dose of 2,400,000 u. or the amount may be divided into 2 injections to be given in two buttocks consecutively.

*Uncomplicated Gonorrhoea in Females.* 2,400,000 u. intramuscularly.

*Gonorrhoea with Complications (eye involvement, prostatitis, arthritis, etc.).* Use aqueous penicillin G 600,000 to 1,200,000 u. per day at 2 to 4 hour intervals, or equivalent doses of repository penicillin until signs and symptoms have subsided.

In the treatment of gonorrhoea, patients with a suspected lesion of syphilis should have darkfield examinations before receiving penicillin and monthly serologic tests for a minimum of three months.

*Supply:* 10 ml. vials of 3,000,000 units (300,000 units per ml.).

*Note:* No refrigeration required. The material may settle somewhat on standing. A brisk shaking readily suspends the contents uniformly.

*Expiration date* 36 months at room temperature.

## PENICILLIN G SODIUM CRYSTALLINE, BUFFERED, SQUIBB — Sterile Powder

Squibb Penicillin G Sodium is crystalline sodium penicillin G as sterile powder, buffered with 4.5% (w/w) Sodium Citrate (calculated as anhydrous). It is suitable for intramuscular and intravenous use as well as for intrapleural or other local instillation.

*Advantages:*

* suitable for intramuscular and intravenous use
* suitable for intrapleural, intra-articular, or other local instillation
* provides high serum concentration of penicillin
* produces rapid effect

*Indications:* Buffered penicillin G is used when rapid effect or high serum concentrations of penicillin are sought. Penicillin is effective only when the causative organism is penicillin-susceptible and dosage is sufficient to produce bacteriostatic or bactericidal concentrations at the site of infection for a period sufficient to allow body defences to eradicate the infections.

*Contraindications:* This drug is contraindicated in individuals with a history of previous hypersensitivity to it.

*Precautions:* As with any antibiotic preparation, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. Constant observation of the patient is essential. Should superinfection occur, the preparation should be discontinued and/or appropriate therapy instituted.

In the treatment of gonorrhoea, where concomitant syphilis is suspected, make darkfield examination before treatment and serologic tests monthly for three months.

*Adverse Reactions:* Adverse reactions due to penicillin have been largely limited to sensitivity phenomena. Such reactions may include urticaria, serum sickness-like reactions (fever, rash, arthralgia), other skin rashes, and rarely, anaphylactoid shock.

They are more likely to occur in individuals with a history of allergy, asthma, hay fever, or urticaria, and in those who have previously demonstrated hypersensitivity to penicillin. Urticarial, serum sickness-like and other skin rash reactions may be controlled by antihistamines and, if necessary, corticosteroids. Whenever such reactions occur, penicillin should be discontinued unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy. Serious anaphylactoid reactions are not controlled by antihistamines, and require such measures as the immediate use of epinephrine, oxygen, and intravenous corticosteroids.

*Administration:* Buffered penicillin G may be given intramuscularly or by continuous intravenous drip. It is also suitable for intrapleural, intra-articular, or other local instillations.

1. *Intramuscular Injection.* Keep total volume of individual injection small. If desired, large doses may be divided and injected into more than one site to reduce the severity of discomfort.

2. *Continuous Intravenous Drip.* Determine the volume of fluid and rate of its administration required by the patient in a 24-hour period in the usual manner for fluid therapy, and add the appropriate daily dosage of penicillin to this fluid. *For example,* if an adult patient requires 2 litres of fluid in 24 hours and a daily dosage of 10 million units of penicillin, add 5 million units to 1 litre and adjust the rate of flow so that the litre will be infused in 12 hours.

3. *Intrapleural or Other Local Infusion.* If fluid is aspirated, give infusion in a volume equal to one-quarter or one-half the amount of fluid aspirated; otherwise, prepare as for intramuscular injection.

*Preparation of Solutions.* Solutions of penicillin should be prepared as follows: Loosen powder. Hold vial horizontally and rotate it *slowly* while directing the stream of diluent against the wall of the vial. Shake vial vigorously after all the diluent has been added. Depending on the route of administration, use sterile pyrogen-free distilled water (Sterile Water for Injection), sterile pyrogen-free isotonic Sodium Chloride Injection or sterile pyrogen-free 5% dextrose solution (Dextrose Injection).

| *Vial Content* | *Desired Concentration* | *Add Diluent* |
|---|---|---|
| 200,000 units | 50,000 units/ml. | 4 ml. |
| | 100,000 units/ml. | 2 ml. |
| | 200,000 units/ml. | 1 ml. |
| 500,000 units | 50,000 units/ml. | 9.8 ml. |
| | 100,000 units/ml. | 4.8 ml. |
| | 250,000 units/ml. | 1.8 ml. |
| 1,000,000 units | 100,000 units/ml. | 9.6 ml. |
| | 200,000 units/ml. | 4.6 ml. |
| | 250,000 units/ml. | 3.6 ml. |

*Dosage:* Dosage varies according to the site and severity of infection and the infecting organisms. Suggested dosages are given in the following table. Higher doses at more frequent intervals may be required when seriousness of infection and response to treatment indicate.

In general, when the infection has been brought under control and the patient is responding to treatment, oral or repository parenteral penicillin preparations may be used in place of buffered penicillin G. Therapy for most infections should be continued until signs of infection are absent and temperature has been normal for at least 48 hours. Streptococcal infections should be treated for a total of 10 days to guard against the risk of rheumatic fever or glomerulonephritis. Bacterial endocarditis should be treated for at least four to six weeks; in some staphylococcal infections prolonged therapy is also required.

## GUIDE TO THERAPY

| *Condition* | *Daily Dosage* | *Comments* |
|---|---|---|
| Severe infections caused by staphylococci (susceptible strains) streptococci pneumococci Clostridia (with antitoxin) *C. diphtheriae* (with antitoxin) Complications of gonorrhoea. | Total of 1,200,000 units to 12,000,000 units in given divided doses q. 2 to 4 h.i.m. or by continuous i.v. drip. | In staphylococcal infections higher dosage may be required; sensitivity tests should be made to determine efficacy of penicillin and/or other antibiotics. Indicated surgical procedures should be carried out in all cases. |
| Bacterial endocarditis Subacute: pneumococcal or streptococcal | Total of 2,400,000 units given in divided doses q. 4 h.i.m. or by continuous i.v. drip | Supplemental administration of streptomycin may be advisable in subacute bacterial endocarditis. |
| Acute: gonococcal or staphylococcal | Total of 24,000,000 units given in divided doses q. 2 h.i.m. or by continuous i.v. drip | |
| Severe and/or due to resistant organisms | Total of 10,000,000 units to 100,000,000 units by continuous i.v. drip | |
| Syphilis | | |
| Infantile congenital (for infants less than 2 years of age) | Total of 100,000 units per lb. body weight, given in divided doses q. 3 h.i.m. for 10 days | For other forms of syphilis use procaine penicillin. |

*Supply:* Vials of 200,000 units — Boxes of 10 vials.
Vials of 500,000 units — Boxes of 10 vials.
Vials of 1,000,000 units — Boxes of 10 vials.

*Expiration date* 24 months. The dry powder is relatively stable and may be stored at room temperature; sterile solutions may be kept in the refrigerator one week without significant loss of potency. Store in a cool, dry place.

## PENMYN®

**Sterile Powder**

## PENMYN® FORTIS

**Sterile Powder**

Squibb Buffered Crystalline Sodium Penicillin G and Streptomycin Sulphate

Penmyn and Penmyn Fortis are supplied as dry powder for aqueous injection. Each vial of Penmyn provides 500,000 units of Buffered Crystalline Sodium Penicillin G and Streptomycin Sulphate equivalent to 0.25 Gm. of the base. Each vial of Penmyn Fortis provides 500,000 units of Buffered Crystalline Sodium Penicillin G and Streptomycin Sulphate equivalent to 0.5 Gm. of the base.

*Indications:* Penmyn and Penmyn Fortis are recommended in the treatment of peritonitis, mediastinitis, suspected brain abscess and other infections in which the causative organisms cannot be identified without unwarranted operative procedures. Whenever possible, however, a thorough search for the primary focus should be made in order to determine if sensitivity to this combination warrants its use. They are also recommended in some mixed infections, particularly those involving gram-positive and gram-negative organisms, e.g., those common in the respiratory or urogenital tract and in contaminated wounds. Penmyn and Penmyn Fortis may be given for prophylaxis in surgery where there is danger of contamination, particularly from the contents of a hollow viscus. They may also be valuable in selected cases of septicaemia caused by enterococci or other organisms susceptible to streptomycin and penicillin, especially if there is *in vitro* evidence that this combination of antibiotics has an additive or synergistic effect. When treatment is prolonged it is wise to perform periodic *in vitro* sensitivity tests to determine any change in the sensitivity of the causative organisms. Penmyn and Penmyn Fortis may be effective in infections where the bacteria are relatively more resistant to penicillin or streptomycin alone than to the combination. Penmyn will be of great value, particularly in paediatric practice, in view of its lower streptomycin content. Children being more prone to streptomycin toxicity, a dose of 20 to 40 mg. of streptomycin per day per kilogram body weight should not be exceeded.

*Dosage:* The dose of Penmyn and Penmyn Fortis should be determined primarily by the currently recommended dosage of streptomycin. The range of dosage is one to two vials of Penmyn or Penmyn Fortis per day. In severe infection the dosage may be doubled. In paediatric practice, a dosage of 20 to 40 mg. streptomycin per day per kilogram body weight will be the optimal range. The best guide to the duration of treatment is provided by the clinical response of the patient. It is recommended that treatment be continued for 3 to 4 days after the temperature has returned to normal or cultures have become consistently negative.

*Administration:* Following dilution in pyrogen-free water or sterile isotonic sodium chloride solution, Penmyn and Penmyn Fortis are administered intramuscularly. For reconstitution add 1.1 ml. of sterile distilled water or sterile normal saline to the vial of Penmyn. 1.5 ml. of diluent is to be used for Penmyn Fortis. The administration is a matter of simple intramuscular injection after aspirating to be sure the needle is not in a vein. Intramuscular injections are sometimes painful.

The pain is reduced if the following precautions are observed:

1. Inject high in the upper outer quadrant of the buttock.
2. Change the site for each injection.
3. Insert needle deeply to avoid subcutaneous deposition.
4. Use 0.5% Xylocaine ‡ as diluent for Penmyn and Penmyn Fortis if necessary.

*Toxicity:* There are two active components in Penmyn and Penmyn Fortis: Penicillin and Streptomycin. It has not been shown that any specific toxicity results from the simultaneous administration of penicillin and streptomycin.

*Penicillin:* Toxic reactions due to penicillin have been largely limited to sensitivity phenomena; such as urticaria (hives) and angioneurotic oedema, should be treated by the customary measures for combating allergy. Antihistaminic drugs are beneficial. Fever and arthralgia do not respond to such therapy but disappear on discontinuance of the drug. If reactions cannot be controlled and are more serious than the condition being treated, discontinue Penmyn.

*Streptomycin:* Streptomycin causes a number of untoward phenomena, particularly injury to nervous system and hypersensitivity reactions. With the usual dosage given for one or two weeks severe toxic effects are rarely produced. The main danger in the chronic use of streptomycin is damage to the eighth cranial nerve manifested chiefly by vestibular disturbances and, at times, by auditory impairment. Vestibular damage may be permanent, although symptoms tend to disappear as the patient adjusts and learns to compensate visually. Auditory impairment, if it occurs, also appears to be permanent.

Skin or allergic reactions occur infrequently and can usually be controlled with antihistaminic agents.

Headache, paraesthesias of the face and gastric disturbances may occur. Clinical judgment as to termination of therapy must be exercised when such side effects occur.

*Supply:* Penmyn and Penmyn Fortis, 1 dose, boxes of 10 vials.

*Expiration date* 24 months. May be stored at room temperature. Sterile solutions may be kept in the refrigerator for one week without loss of potency.

**PENTIDS®** **Tablets**

Squibb Penicillin G Potassium 200,000 Units

**PENTIDS® '400'** **Tablets**

Squibb Penicillin G Potassium 400,000 Units

‡ 'Xylocaine' is a trade mark of Astra Pharmaceutical Products, Inc. for Lidocaine.

Pentids and Pentids '400' are scored, compressed, uncoated tablets for oral administration. Each Pentids Tablet contains 125 mg. (200,000 units) crystalline penicillin G potassium, and each Pentids '400' Tablet contains 250 mg. (400,000 units). Both are buffered with calcium carbonate.

*Action:* Studies conducted in human subjects indicate that, following oral administration, potassium penicillin G is readily absorbed from the gastrointestinal tract; the desired elevated blood levels are achieved rapidly. The efficacy of potassium penicillin G has been established by clinical studies in many millions of patients. Pentids cause few gastrointestinal side effects; hypersensitivity reactions following oral administration of penicillin are much less common than with parenteral use of the drug.

*Advantages:*

* economical
* readily absorbed from the gastrointestinal tract
* rapidly achieves desired blood levels
* few gastrointestinal side effects

*Indications:* Pentids are indicated for the oral treatment of mild to moderately severe infections due to penicillin-susceptible organisms, including haemolytic streptococcal infections such as scarlet fever, erysipelas, tonsillitis and sinusitis, lymphadenitis, mastoiditis and otitis media; minor infections due to susceptible staphylococci and without bacteraemia; pneumococcal infections; Vincent's stomatitis and pharyngitis; and gonorrhoea. Pentids may also be used for the prophylaxis of rheumatic fever. If the infections do not respond promptly, parenteral penicillin should be administered, or other appropriate medication substituted. In dentistry, Pentids are indicated for the oral treatment of penicillin-susceptible infections that may occur after tooth extraction or other dental surgery. Pentids are useful as adjunctive therapy in pericoronitis, alveolitis, dentoalveolar abscess and cellulitis.

*Contraindications:* Like other oral penicillin preparations, Pentids are not recommended in syphilis, subacute bacterial endocarditis, or meningitis and are contraindicated in individuals who have shown hypersensitivity to penicillin.

*Precautions:* As with any antibiotic preparation, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. Constant observation of the patient is essential. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted.

*Adverse Reactions:* Diarrhoea or epigastric distress is generally not a problem with oral penicillin therapy. Loose stools may be encountered, but this condition is usually less severe, and certainly less frequent, than with broad spectrum antibiotic therapy. Untoward reactions are essentially limited to sensitivity phenomena. Such reactions are less common with oral administration, but may include urticaria, serum sickness-like reactions (fever, rash, arthralgia), other skin rashes, and rarely, anaphylactoid shock. They are more likely to occur in individuals with a history of allergy, asthma, hay fever, or urticaria, and in those who have previously demonstrated hypersensitivity to penicillin.

Urticarial, serum sickness-like and other skin rash reactions may be controlled by antihistamines and, if necessary, corticosteroids. Whenever such reactions occur, penicillin should be discontinued unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy. Serious anaphylactoid reactions are not controlled by antihistamines, but require such measures as the immediate use of epinephrine, oxygen, and intravenous corticosteroids.

*Dosage:* Penicillin dosage for children is not predicated on a weight basis but is the same as that for adults. The following dosage schedule is suggested:

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|---|---|
| Haemolytic streptococcal infections: scarlet fever, erysipelas, tonsillitis, otitis media, sinusitis, pharyngitis, lymphadenitis, mastoiditis | 400,000 units t.i.d. Treatment should be continued for 10 full days to guard against the risk of rheumatic fever or glomerulonephritis. |
| Pyogenic skin infections<br>Pneumococcal infections | 200,000 or 400,000 units t.i.d. |
| Minor staphylococcal infections (susceptible to oral therapy and without bacteraemia.) | 400,000 units t.i.d. in conjunction with indicated surgical measures. |
| Gonorrhoea | 200,000 units t.i.d. for 2 or 3 days.<br>When concomitant syphilis is suspected, make darkfield examinations before treatment and monthly serologic tests for a minimum of three months. |
| Vincent's angina | 200,000 units t.i.d. |
| Prevention of streptococcal infections in individuals with a history of rheumatic fever | 200,000 units once or twice daily for an indefinite period. Twice daily is probably more effective. |

**For maximum absorption of penicillin, dosage should be given on an empty stomach.** Thus, doses of 200,000 units should be given ½ hour before or at least 2 hours after meals. The blood concentration with doses of 400,000 units is sufficiently high to inhibit sensitive bacteria when the tablets are given without regard to meals but, as can be expected, the resultant concentration will be higher when they are given before meals.

*Supply:* Pentids: Boxes of 48 tablets (8 strips of 6's).
Pentids '400': Boxes of 48 tablets (8 strips of 6's).

*Note:* Store in a cool, dry place.

*Expiration date* 24 months.

## PENTIDS® '800'

**Tablets**

Squibb Penicillin G Potassium 800,000 Units

Pentids '800' Tablets are scored, compressed, uncoated tablets for oral administration. Each Pentids '800' Tablet contains 500 mg. (800,000 units) crystalline potassium penicillin G. It is buffered with calcium carbonate.

*Action:* Penicillin G is a bactericidal antibiotic. Its bactericidal action is exerted against penicillin sensitive microorganisms. It is not active against penicillinase producing bacteria, viz. certain strains of staphylococci. Following oral administration, potassium penicillin G is readily absorbed from gastrointestinal tract. Addition of buffer increases the stability of antibiotic in the gastric content. Absorption occurs mainly in the duodenum and blood levels are achieved rapidly, usually within a period of 30 to 60 minutes. Fewer gastrointestinal side effects, rapid absorption, rapid achievement of desired blood levels and rare hypersensitivity reactions following oral administration are the main advantages of Pentids '800'.

*Indications:* Pentids '800' Tablets are indicated for oral treatment of mild to moderately severe infections due to penicillin susceptible microorganisms. These include haemolytic streptococcal infections such as scarlet fever, erysipelas, tonsillitis, sinusitis, lymphadenitis, mastoiditis and otitis media; infections due to susceptible strains of staphylococci without bacteraemia; pneumococcal infections; Vincent's stomatitis and pharyngitis; and gonorrhoea. Pentids '800' may also be used for the prophylaxis of streptococcal infections in individuals with a history of rheumatic fever and to prevent bacterial endocarditis in patients with congenital or rheumatic heart lesions who are to undergo dental surgery or minor upper respiratory tract surgery.

*Contraindications:* It is contraindicated in patients with a history of hypersensitivity to any penicillin.

*Precautions:* Prolonged use may result in superinfection. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted.

*Adverse Reactions:* Loose stools may be encountered, but this is less severe and less frequent than with broad spectrum antibiotics. Other less frequent symptoms include nausea, vomiting, epigastric distress and black hairy tongue. Untoward reactions are limited to sensitivity phenomena. Such reactions are less common with oral administration. Urticaria, fever, rash, arthralgia and rarely anaphylactic shock may be encountered. These are more likely to occur in individuals with a history of allergy and in those patients who have previously demonstrated hypersensitivity to penicillin. Whenever severe hypersensitivity reactions occur, penicillin therapy should be discontinued and appropriate therapy instituted.

*Dosage:* Severity of the infection, therapeutic response and the sensitivity of causative organisms are the primary criteria by which the dosage of Pentids '800' is established in treatment of individual patient. For mild to moderately severe streptococcal infections of the upper respiratory tract and including otitis media, scarlet fever and mild erysipelas, one tablet may be given two times daily for ten days.

For other infections, one to two tablets of Pentids '800' given twice daily will usually suffice. Alternatively, one tablet may be given t.i.d.

For medical conditions in which oral penicillin therapy is indicated as a prophylaxis, half tablet may be given on a continuing basis for prevention of recurrence of rheumatic fever and/or chorea.

To prevent bacterial endocarditis in patients with congenital or rheumatic heart lesions who are to undergo dental procedure or minor upper respiratory tract surgery or instrumentation, ½ tablet given on day of procedure; 500,000 units aqueous penicillin G intramuscular an hour prior to procedure and half tablet t.i.d. for two more days will suffice.

*Supply:* Pentids '800': Boxes of 48 tablets (12 strips of 4's).

*Note:* Store in a cool, dry place.

*Expiration date* 24 months.

## PENTIDS® FOR SYRUP — Powder for Syrup

Squibb Penicillin G Potassium

Pentids for Syrup is Squibb Penicillin G Potassium for infants and children. Each 5 ml. contains 125 mg. (200,000 units) crystalline penicillin G Potassium buffered with Sodium Phosphates.

*Action:* Following oral administration potassium penicillin G is readily absorbed from the gastrointestinal tract. Addition of buffer material increases the stability of the antibiotic in the gastric content. Absorption occurs mainly in the duodenum and the desired elevated blood levels are achieved rapidly within a period of 30 to 60 minutes. Oral preparations of penicillin G are only slightly affected by normal gastric acidity (pH 2-3.5) however a pH below 2.0 may partially inactivate penicillin. Excretion occurs mainly through the kidney. Approximately 60% of penicillin G is bound to serum proteins. The drug is widely distributed through the body tissues in varying amounts. Penicillin G penetrates into all other tissues with very limited amounts found in the cerebrospinal fluid.

Penicillin G is bactericidal against penicillin-sensitive microorganisms. It is not active against the penicillinase producing bacteria, viz. some strains of staphylococci.

*Advantages:*

* economical
* readily absorbed from the gastrointestinal tract
* rapidly achieves desired blood levels
* few gastrointestinal side effects

*Indications:* Pentids for Syrup is indicated in the treatment of mild to moderately severe infections due to penicillin G sensitive microorganisms. Therapy should

be guided by bacteriological studies including sensitivity tests and clinical response. The susceptible organisms which will respond to adequate dosage of Pentids for Syrup include Streptococcal Group A infections of upper respiratory tract, skin and soft tissues, scarlet fever, mild erysipelas; pneumococcal infections of the respiratory tract; staphylococcal infections of skin and soft tissues excluding penicillinase-producing strains, Vincent's gingivitis and pharyngitis.

Pentids for Syrup can also be employed for prophylaxis against recurrence following rheumatic fever and chorea, to prevent bacterial endocarditis in patients with congenital and/or rheumatic heart lesions, who are to undergo dental procedures or minor upper respiratory tract surgery such as tonsillectomy, sinus puncture or instrumentation such as laryngoscopy, bronchoscopy or catheterization.

*Contraindications:* It is contraindicated in patients with a history of hypersensitivity to any penicillin.

*Warning:* Severe pneumonia, empyema, bacteraemia, pericarditis, meningitis, bacterial endocarditis and septic arthritis should not be treated with oral penicillin G during the acute stage.

*Precautions:* Prolonged use in some cases may result in overgrowth of nonsusceptible organisms including fungi. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted. The use of Pentids for Syrup cannot be relied upon in patients with severe illness or with nausea, vomiting, gastric dilatation and intestinal hypermotility. With prolonged therapy with penicillin and particularly with high dosage schedule, periodic evaluation of renal and haematopoietic systems is recommended.

*Adverse Reactions:* Serious and occasional fatal hypersensitivity reactions have been reported in patients on penicillin therapy. Although these are much less frequent with Pentids for Syrup, this hazard has to be borne in mind. Cross hypersensitivity with cephalosporins has also been observed. Other allergic reactions like serum sickness and urticaria have been reported more in such patients with history of allergy, asthma and hay fever. In such cases, the syrup should be discontinued and appropriate therapy instituted. Loose stools may be encountered in a few cases. Other less frequent symptoms include nausea, vomiting, epigastric distress and black hairy tongue.

*Administration and Dosage:* Therapy for children under 12 years of age is calculated on the basis of body weight. For infants and small children the suggested dose is 15-56 mg. (25,000-90,000 units) per Kg./day in 3 to 6 divided doses. It should be given at least 1 to 2 hours after meals.

For mild streptococcal infections 5 ml. of Pentids for Syrup containing 200,000 units t.i.d. for 10 days is recommended; while for moderate to severe infections a higher dose of 10 ml. (400,000 units) may be employed t.i.d. For mild to moderate pneumococcal infections of the respiratory tract, 10 ml. (400,000 units) t.i.d. of Pentids for Syrup till two days after the fever has touched normal is the usual course of treatment. 5 ml. to 10 ml. of Pentids for Syrup t.i.d. is advisable for staphylococcal infections of skin and soft tissues, Vincent's gingivitis and pharyngitis until infection is cured.

For medical prophylaxis against recurrence following rheumatic fever/chorea 5 ml. twice daily on a continuing basis is advocated. To prevent bacterial endocarditis in patients with congenital or rheumatic heart lesions who are to undergo dental procedures or minor upper respiratory tract surgery or instrumentation 5 ml. of Pentids for Syrup is given every 6 hours for 2 days, prior to surgery, on the day of operation and for 2 days afterwards. In addition to this an intramuscular injection of 600,000 units of aqueous penicillin G is given one hour prior to the procedure.

*Directions for preparing the syrup:* A cup to measure 27 ml. of water has been provided with this pack. Fill this cup with boiled and cooled water, add it to the contents and shake well. This will make the final volume of syrup to 60 ml. One spoon enclosed will measure 5 ml. containing 125 mg. (200,000 units) of potassium penicillin G. Total volume of syrup provides 12 doses, each containing 200,000 units of penicillin G potassium.

*Supply:* Pentids for Syrup is available for oral administration as powder which when reconstituted as directed provides 60 ml. of fruit flavoured syrup. Each 5 ml. (spoon measure) contains 125 mg. (200,000 units) of potassium penicillin G. One such bottle of reconstituted syrup provides in all 12 doses.

*Note:* Reconstituted material should be used up within 3days. Store dry powder in a cool, dry place.

*Expiration date* 15 months.

## PENTID-SULFAS® — Tablets

## PENTID-SULFAS® FOR SYRUP — Powder for Syrup

Squibb Penicillin with Triple Sulphas

Pentid-Sulfas is Squibb Penicillin with Triple Sulphas, a penicillin-sulphonamide combination formulated for convenient q.i.d. dosage. Each Pentid-Sulfas Tablet provides 125 mg. (200,000 units) penicillin G potassium and 0.5 Gm. Trisulphapyrimidines (167 mg. each of sulphadiazine, sulphamethazine, and sulfamerazine).

Pentid-Sulfas for Syrup (buffered penicillin powder with sulphadiazine, sulphamethazine and sulfamerazine) is particularly useful in treating infants and children. When prepared with water, the preparation provides a fruit-flavoured suspension with a potency of 125 mg. (200,000 units) potassium penicillin G and 0.5 Gm. trisulphapyrimidines (167 mg. each of sulphadiazine, sulphamethazine and sulfamerazine) per 7.5 ml. (spoonful). The preparation is buffered with sodium phosphates.

*Action*: The combination of penicillin and sulphonamides provides the bactericidal activity of penicillin against gram-positive and some gram-negative organisms plus the effective action of the sulphas against gram-positive and gram-negative organisms. The use of combined sulphadiazine, sulphamethazine, and sulfamerazine provides fully adequate sulphonamide blood concentrations and minimizes the danger of crystalluria or renal damage.

*Advantages:*

* provides the bactericidal activity of penicillin plus the effective action of the sulphas against gram-positive and gram-negative organisms
* minimizes danger of crystalluria and renal damage

*Indications:* Pentid-Sulfas Tablets and Pentid-Sulfas for Syrup are indicated for mixed infections and for those infections that can be expected to respond better to the combination than to penicillin or the sulphonamides alone. These include urinary tract infections due to susceptible gram-negative organisms.

Pentid-Sulfas may be valuable as an adjuvant to parenteral penicillin in the treatment of some cases of coccal meningitis.

The preparations are not recommended for infections which usually respond to the full doses of either penicillin or sulphonamides alone. Bacteriologic diagnosis and sensitivity tests will provide appropriate guides to therapy in this respect.

*Contraindications:* These preparations should not be used in patients with a history of penicillin and/or sulpha drug sensitivities, in pregnant females at term, in premature infants or in newborn infants during the first week of life.

*Warning:* The preparations should be used only after critical appraisal in patients with liver damage, renal damage, urinary obstruction, or blood dyscrasias. Deaths have been reported from hypersensitivity reactions, agranulocytosis, aplastic anaemia, and other blood dyscrasias associated with sulphonamide administration. When used intermittently, or for a prolonged period, blood counts and liver and kidney function tests should be performed.

*Precautions:* These preparations should be used with caution in persons having histories of significant allergies and/or asthma. Streptococcal infections should be treated for a minimum of 10 days to guard against the risk of rheumatic fever or glomerulonephritis. The usual precautions adopted in routine sulphonamide therapy should also be observed with use of these preparations. The patient should be kept under close supervision. Although haematuria, crystalluria, or renal blockage are infrequent with trisulphapyrimidine therapy, adequate fluid intake is necessary. If urine volume is low, fluids should be forced in order to avoid the possibility of intratubular blockage. It may be advisable in some instances to administer alkalis sufficient to achieve a urinary pH of 7 or higher.

*Adverse Reactions:* Diarrhoea or epigastric distress is generally not a problem with oral penicillin therapy. Loose stools may be encountered, but this condition is usually less severe, and certainly less frequent than with broad spectrum antibiotic therapy. Untoward reactions are essentially limited to sensitivity phenomena. Such reactions are less common with oral administration but may include urticaria, serum sickness-like reactions (fever, rash, arthralgia), other skin rashes, and rarely, anaphylactoid shock. They are more likely to occur in individuals with a history of allergy, asthma, hay fever, or urticaria, and in those who have previously demonstrated hypersensitivity to penicillin.

Urticarial, serum sickness-like, and other skin rash reactions may be controlled by antihistamines and, if necessary, by corticosteroids. Whenever such reactions occur, penicillin should be discontinued unless in the opinion of the physician, the condition being treated is life-threatening and amenable only to penicillin therapy. Serious anaphylactoid reactions are not controlled by antihistamines, and require such measures as the immediate use of epinephrine, oxygen, and intravenous corticosteroids.

As in all sulphonamide therapy, the following reactions may occur: nausea, vomiting, diarrhoea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, urticaria or skin rash, injection of the conjunctiva and sclera, petechiae, purpura, haematuria, and crystalluria. The dosage should be decreased or the drug withdrawn depending upon the severity of the reaction.

As with any antibiotic preparation, prolonged use may result in overgrowth of non-susceptible organisms, including fungi. Constant observation of the patient is essential. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted.

An occasional patient may complain of sore mouth or tongue, as with any oral penicillin preparation.

*Dosage:* The suggested adult dosage is 2 tablets or 2 spoonfuls Pentid-Sulfas for Syrup q.i.d. If a priming dose is desired 7 or 8 tablets or 7 or 8 spoonfuls of Pentid-Sulfas for Syrup are suggested.

The daily paediatric dosage should supply 140 to 220 mg. trisulphapyrimidines per Kg. of body weight in divided doses given every 4 to 6 hours.

Pentid-Sulfas preparations should be taken ½ hour before or two hours after meals, and at bedtime. Fluid intake should be adequate as with ordinary sulphonamide therapy.

In overwhelming infections, or when the response of the patient is not prompt, the supplemental use of parenteral penicillin or another antibiotic is advised.

The following dosage regimens are suggested:

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| Haemolytic streptococcal infections: scarlet fever, tonsillitis, otitis media, sinusitis, pharyngitis, lymphadenitis, mastoiditis. | 1 tablet or spoonful q.i.d. Treatment should be continued for 10 full days to guard against the development of rheumatic fever or glomerulonephritis. |
| Pneumococcal infections | 1 or 2 tablets or spoonfuls q.i.d. |
| Staphylococcal infections (susceptible to oral therapy) | 2 tablets or spoonfuls q.i.d. in conjunction with indicated surgical measures. |
| Gonorrhoea | 1 tablet or spoonful b.i.d. for 2 or 3 days. |
| Urinary tract infections<br>Prophylaxis against secondary infection due to penicillin or sulphonamide-susceptible organisms. | 1 tablet or spoonful q.i.d. |

*Supply:* Pentid-Sulfas Tablets: Boxes of 48 tablets (8 strips of 6's).

*Note:* Store in a cool, dry place.

*Expiration date* 24 months.

Pentid-Sulfas for Syrup: Bottles containing 61 Gm. powder which when reconstituted with 55 ml. of boiled and cooled or distilled water gives 90 ml. syrup.

*Expiration date* 18 months. Store dry powder at room temperature. Reconstituted material should be used up within 3 days.

## PHOSFOMIN®

**Elixir**

Squibb Multiple Glycerophosphates Elixir with B Complex Vitamins

Phosfomin is Squibb Multiple Glycerophosphates Elixir with B Complex Vitamins. Each fluid ounce (approximately 30 ml.) of pleasantly-flavoured Phosfomin provides:

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| Calcium Glycerophosphate | 220 mg. |
| Sodium Glycerophosphate | 160 mg. |
| Potassium Glycerophosphate | 40 mg. |
| Manganese Glycerophosphate | 20 mg. |
| Vitamin $B_1$ (Thiamine Mononitrate) | 4 mg. |
| Vitamin $B_2$ (Riboflavine) | 2 mg. |
| Vitamin $B_6$ (Pyridoxine Hydrochloride) | 1 mg. |
| Niacinamide | 30 mg. |
| d-Panthenol | 2 mg. |
| Vitamin $B_{12}$ activity | 30 mcg. |

Alcohol content: 11% by volume

*Indications:* Phosfomin combines certain B Complex vitamins, which stimulate general metabolism and appetite with glycerophosphates, which have been used for some years as a tonic stimulant. The product is recommended for its tonic effect in nervous and debilitating disorders. It improves the appetite and digestive functions, tends to correct B Complex deficiencies and also increases and improves the general physical well-being of the patient.

*Dosage:* The recommended dosage of Phosfomin is 1 tablespoonful 3 times a day or as directed by the physician.

*Supply:* Bottles of 240 ml. and 480 ml.

*Note:* Bottles of Phosfomin should be kept tightly closed; they should not be exposed to sunlight.

*Expiration date* 24 months.

## PHOSFOMIN® IRON — Elixir

Squibb Multiple Glycerophosphates Elixir with B Complex Vitamins and Iron

Phosfomin Iron is Squibb Multiple Glycerophosphates Elixir with B Complex Vitamins and Iron.

Each 15 ml. of pleasantly flavoured Phosfomin Iron provides:

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| Calcium Glycerophosphate | 110 mg. |
| Sodium Glycerophosphate | 80 mg. |
| Potassium Glycerophosphate | 20 mg. |
| Manganese Glycerophosphate | 10 mg. |
| Ferric ammonium citrate I.P. | 46.5 mg. |
| Vitamin $B_1$ (Thiamine Mononitrate) | 2 mg. |
| Vitamin $B_2$ (Riboflavine) | 1 mg. |
| Vitamin $B_6$ (Pyridoxine Hydrochloride) | 0.5 mg. |
| Niacinamide | 15 mg. |
| d-Panthenol | 1 mg. |
| Vitamin $B_{12}$ activity | 15 mcg. |
| Alcohol I.P. | 1.75 ml. |

Extra Vitamins added to compensate for loss on storage.
Alcohol content: 11% by volume.

*Indications:* Phosfomin Iron combines multiple glycerophosphates, B Complex vitamins and Iron which are essential for the general well-being of the patient. It improves appetite and digestive functions, stimulates general metabolism and corrects certain B Complex deficiencies. Supplementary iron in Phosfomin Iron tends to compensate the iron loss in women during menstruation and other physiological stress conditions. The product is recommended for its tonic effects on nervous and debilitating disorders, and for the overall general well-being of the patient.

*Dosage:* The recommended dosage of Phosfomin Iron is 1 tablespoonful 3 times a day or as directed by the physician.

*Supply:* Bottles of 240 ml. and 480 ml.

*Note:* Bottles of Phosfomin Iron should be kept tightly closed, they should not be exposed to sunlight.

*Expiration date* 24 months.

## PRONESTYL® HYDROCHLORIDE — Tablets, Parenteral Solution

Squibb Procainamide Hydrochloride

Pronestyl is the amide analogue of procaine hydrochloride. It is available as tablets supplying 0.25 Gm. for oral use and as a 10% sterile aqueous solution (100 mg./ml.) for parenteral use.

The parenteral solution contains 0.9% (w/v) benzyl alcohol and 0.1% sodium metabisulphite as preservatives; the pH has been adjusted to 4.0–6.0 with hydrochloric acid or sodium hydroxide. The solution, which is colourless initially, may in time develop a slightly yellow colour. This does not indicate a change which would prevent its use, but a solution any darker than light amber or discoloured in any other way should not be used. At the time of manufacture, the air in the container is replaced by nitrogen.

*Action:* Procainamide depresses the excitability of cardiac muscle to electrical stimulation, and slows conduction in the atrium, the bundle of His, and the ventricle. The refractory period of the atrium is considerably more prolonged than that of the ventricle. Contractility of the heart is usually not affected nor is cardiac output decreased to any extent unless myocardial damage exists. In the absence of any arrhythmia, the heart rate may occasionally be accelerated by conventional doses, suggesting that the drug possesses anticholinergic properties. Larger doses can induce atrioventricular block and ventricular extrasystoles which may proceed to ventricular fibrillation. These effects on the myocardium are reflected in the electrocardiogram; a widening of the QRS complex occurs most consistently; less regularly, the P-R and Q-T intervals are prolonged, and the QRS and T waves show some decrease in voltage.

The action of procainamide begins almost immediately after intramuscular or intravenous administration. Plasma levels after intramuscular injection are at their peak in 15 to 60 minutes. Following oral administration, plasma levels of the drug are comparable to those obtained parenterally and are maximal within an hour; therapeutic levels are usually attained in half that time.

Procainamide is less readily hydrolyzed than procaine, and plasma levels decline slowly—about 10% to 20% per hour. The drug is excreted primarily in the urine, about 10% as free and conjugated *p*-aminobenzoic acid and about 60% in the unchanged form. The fate of the remainder is unknown.

*Indications:* Pronestyl Injection (Squibb Procainamide Hydrochloride Injection) is indicated in the treatment of ventricular extra-systoles and tachycardia, atrial fibrillation, paroxysmal atrial tachycardia, and cardiac arrhythmias associated with anaesthesia and surgery.

Pronestyl Tablets (Squibb Procainamide Hydrochloride Tablets) are indicated in the treatment of premature ventricular contractions and ventricular tachycardia, atrial fibrillation, and paroxysmal atrial tachycardia.

*Contraindications:* It has been suggested that procainamide be contraindicated in patients with myasthenia gravis. Hypersensitivity to the drug is an absolute contraindication; in this connection, cross sensitivity to procaine and related drugs must be borne in mind. Procainamide should not be administered to patients with complete atrioventricular heart block. Procainamide is also contraindicated in cases of high-degree A-V block unless an electrical pacemaker is operative.

*Precautions:* During administration of the drug, evidence of untoward myocardial responses should be carefully watched for in all patients. In the presence of an

abnormal myocardium, procainamide may at times produce untoward responses. In atrial fibrillation or flutter, the ventricular rate may increase suddenly as the atrial rate is slowed. Adequate digitalization reduces, but does not abolish this danger. If myocardial damage exists, ventricular tachysystole is particularly hazardous. Correction of atrial fibrillation, with resultant forceful contractions of the atrium, may cause a dislodgement of mural thrombi and produce an embolic episode. However, it has been suggested that in a patient who is already discharging emboli, procainamide is more likely to stop than to aggravate the process.

Attempts to adjust the heart rate in a patient who has developed ventricular tachycardia during an occlusive coronary episode should be carried out with extreme caution. Caution is also required in marked disturbances of atrioventricular conduction such as A-V block, bundle branch block, or severe digitalis intoxication, where the use of procainamide may result in additional depression of conduction and ventricular asystole or fibrillation.

Parenteral administration should be monitored electrocardiographically whenever practicable. If electrocardiograms give evidence of impending heart block, parenteral administration should be discontinued at once. Since patients with severe organic heart disease and ventricular tachycardia may also have complete heart block which is difficult to diagnose under these circumstances, this complication should always be kept in mind when treating ventricular arrhythmias with procainamide (especially parenterally). If the ventricular rate is significantly slowed by procainamide without attainment of regular atrioventricular conduction, the drug should be stopped and the patient re-evaluated since asystole may result under these circumstances.

In patients receiving normal dosage, but who have both liver and kidney disease, symptoms of overdosage (principally ventricular tachycardia and severe hypotension) may occur due to drug accumulation.

Instances of a syndrome resembling lupus erythematosus have been reported in connection with maintenance procainamide therapy. The mechanism of this syndrome is uncertain. Polyarthralgia, arthritis, and pleuritic pain are common symptoms; to a lesser extent fever, myalgia, skin lesions, pleural effusion and pericarditis may occur. Rare cases of thrombocytopenia or Coombs positive haemolytic anaemia have been reported which may be related to this syndrome. Patients receiving procainamide for extended periods of time or in whom symptoms suggestive of a lupus-like reaction appear should have antinuclear antibody titres measured at regular intervals. The drug should be discontinued if there is a rising titre (anti-nuclear antibody) or clinical symptoms of LE appear. The LE syndrome may be reversible upon discontinuation of the drug. If discontinuation of the drug does not cause remission of the symptoms, steroid therapy may be effective. If the syndrome develops in a patient with recurrent life-threatening arrhythmias not controllable by other antiarrhythmic agents, steroid suppressive therapy may be used concomitantly with procainamide.

*Adverse Reactions:* Because procainamide is a peripheral vasodilator, intravenous administration may produce transient but at times severe lowering of blood

pressure, particularly in conscious patients. Intramuscular injection is less likely to be accompanied by serious falls in blood pressure, and hypotension following oral administration is rare. Serious disturbances of cardiac rhythm such as ventricular asystole or fibrillation are also more common with intravenous administration. Precautionary measures to be followed during intravenous administration are given in the section on *"Administration and Dosage"*.

Large oral doses of procainamide may sometimes produce anorexia, nausea, urticaria, and/or pruritus.

A syndrome resembling lupus erythematosus has been reported (See *"Precautions"*). Reactions consisting of fever and chills have also been reported, including a case with fever and chills plus nausea, vomiting, abdominal pain, acute hepatomegaly, and a rise in serum glutamic oxaloacetic transaminase following single doses of the drug. Bitter taste, diarrhoea, weakness, mental depression, giddiness, and psychosis with hallucinations have been reported. The possibility of such untoward effects should be borne in mind.

Hypersensitivity reactions such as angioneurotic oedema and maculopapular rash have also occurred.

Agranulocytosis has occasionally followed the repeated use of the drug, and deaths have occurred. Therefore, routine blood counts are advisable during maintenance procainamide therapy. The patient should be instructed to report any soreness of the mouth, throat, or gums, unexplained fever or any symptoms of upper respiratory tract infection. If any of these should occur, and leucocyte counts indicate cellular depression, procainamide therapy should be discontinued and appropriate treatment should be instituted immediately.

*Administration and Dosage:* Oral administration is preferred. When parenteral therapy is necessary, intramuscular administration is the method of choice. *Intravenous use should be limited to extreme emergencies.*

If procainamide therapy is continued for appreciable periods, electrocardiograms should be made occasionally to determine the need for the drug.

*Oral dose:* For ventricular tachycardia, an initial dose of 1 gramme orally followed thereafter by a *total daily dose* of 50 mg./Kg. of body weight given at 3 hour intervals. The suggested oral dosage for premature ventricular contractions is 50 mg./Kg. of body weight daily given in divided doses at 3 hour intervals.

**To provide 50 mg./Kg./day:** Give patients weighing less than 120 lbs., 250 mg. q. 3 hours; give patients between 120 and 200 lbs., 375 mg. q. 3 hours; and give patients over 200 lbs., 500 mg. q. 3 hours. This dosage schedule is for use as a guide for treating the average patient but all patients must be considered on an individual basis.

In atrial fibrillation and paroxysmal atrial tachycardia, an initial dose of 1.25 g. may be followed in one hour by 0.75 g. if there have been no electrocardiographic changes. A dose of 0.5 to 1 g. may then be given every 2 hours until arrhythmia is interrupted or the limit of tolerance is reached. Suggested maintenance dosage is 0.5 to 1 g. every 4 to 6 hours.

*Intramuscular dose:* If the oral route is not feasible, 0.5 to 1 g. may be given intramuscularly, repeated every 6 hours until oral therapy is possible.

*Intravenous dose:* The usual intravenous dose for ventricular extrasystoles and tachycardia ranges from 0.2 to 1 g.; for atrial fibrillation and paroxysmal atrial tachycardia, the intravenous dose averages 0.5 g. although up to 1 g may be required.

*Caution:* Intravenous use of procainamide is accompanied by a hypotensive response, sometimes precipitous. For this reason, the intravenous dose should not exceed 1 g., and should be diluted to permit greater control of infusion rate. It should be administered at a rate not exceeding 25 to 50 mg. per minute. Intravenous infusion should be monitored electrocardiographically, so that the infusion may be stopped when the arrhythmia is interrupted or when excessive widening of the QRS complex or prolongation of the P-R interval suggests the occurrence of myocardial toxicity. Patients should be kept in a supine position and blood pressure should be measured almost continuously during the infusion. If the fall in blood pressure exceeds 15 mm. Hg., the infusion should be temporarily discontinued. Solutions of Phenylephrine Hydrochloride Injection U.S.P. should be available to counteract severe hypotensive responses.

*Surgical Use:* For cardiac arrhythmias associated with anaesthesia and surgery, the suggested parenteral dose is 0.1 to 0.5 g., preferably given intramuscularly.

*Supply:* Tablets, 0.25 Gm., bottles of 25.
Parenteral Solution, 100 mg. per ml., vials of 10 ml.

*Expiration date* 12 months for Pronestyl Injection.

## QUIXALIN® — Tablets

Squibb Halquinol

Quixalin Tablets provide Squibb Halquinol (chlorhydroxyquinoline) in tablet form for oral administration in the treatment of certain alimentary tract infections. Each Quixalin Tablet contains 0.25 Gm. of Halquinol.

*Action:* Quixalin has been found to exhibit a high order of activity against a wide variety of organisms commonly responsible for enteric infections, including both gram-positive and gram-negative bacteria, many fungi, and certain protozoa.[1,2] When tested *in vitro*, Quixalin was found to show a markedly greater inhibitory activity than other halogenated oxines against such common enteric bacilli as *Salmonella* (various species), *Shigella* (various species), and *Escherichia coli;* as well as *Proteus vulgaris, Staphylococcus aureus, Streptococcus faecalis,* and *Streptococcus bovis.* When tested against fungi, Quixalin proved to have a relatively wide range of antifungal activity, showing an inhibitory effect on *Candida albicans,* Epidermophyton floccosum, *Trichophyton mentagrophytes,* several *Microsporum* species, and several *Aspergillus* species. Quixalin has a direct inhibitory effect on *Endamoeba histolytica in vitro.*

Excellent clinical results have been obtained with Quixalin in many common bacterial and amoebic bowel infections in patients of all age groups. After oral administration of Quixalin, the faeces become more solid, the bowel movements less frequent, and tenesmus is diminished within a few days. In most cases, clinical and microbiological cure can be expected. The drug is well tolerated. In the rare instances when side effects occur, these are mild and minor in nature.

*Indications:* Quixalin Tablets are indicated in the treatment of intestinal amoebiasis, bacillary dysentery, and non-specific diarrhoea, i.e., diarrhoeal conditions for which the causative organisms have not been identified.

If specific diagnosis has not yet been made and the patient shows no improvement after 24 hours on the recommended dosage, identification of the causative organisms may be necessary for the consideration of additional therapeutic measures.

*Advantages:*

* combats all three main groups of diarrhoea, i.e., amoebic, bacterial and non-specific
* tolerance is excellent
* no specific contraindications
* side reactions are minor and rare
* no danger of gastric irritation or kidney or liver damage as with iodine or arsenic compounds

*Dosage and Administration:* For adults, 1-2 tablets (0.25-0.5 Gm.) given 3 or 4 times daily are usually adequate. Higher dosages, up to a daily total of 12 to 16 tablets (3 to 4 Gms.) in divided doses, may be required when symptoms are severe or of long duration.

Treatment of intestinal amoebiasis should be continued for 14 days. In certain cases of intestinal amoebiasis, two courses of treatment may be necessary.

In children, upto 40 Kg. of body weight, the recommended total daily dose is 30 to 50 mg. per kilogram of body weight in 3 or 4 divided doses depending on the severity of the infection. The total adult daily dose of 1.5 to 2.0 grammes in 3 or 4 divided doses may be administered to children weighing 40 Kg. or more. Duration of treatment depends upon the disease entity being treated, but should not exceed 14 days for any one course of treatment.

*Side Effects and Precautions:* The only undesirable reactions that have occurred with Quixalin Tablets have been a few instances of nausea and a mild rash in a few patients suggestive of possible sensitivity.

In children, under 2 years of age, diarrhoea may cause rapid and profound changes in water and electrolyte balance. The administration of drugs in these circumstances requires overall evaluation of the patient with particular attention to excretory mechanism. Correction of water and electrolyte balance may be of primary concern.

*Contraindications:* There are no known contraindications. Quixalin, however, is not recommended in typhoid fever, severe fulminating bacillary dysentery or systemic infections.

*Supply:* Boxes of 500 tablets (50 strips of 10's).

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*References:*

1. Heselrine, W. W. and Campbell, P. J.: Laboratory Studies on Chlorhydroxyquinoline, J. Trop. Med. 63: (1960).
2. Neogy, K. N. and Nandy, P. K.: Spectrum of Activity of Quixalin against Enteropathogenic Bacteria. Bull. Calcutta Sch. Trop. Med. 13: 131 (1965).

## RAUDIXIN® Tablets

Squibb Standardized Whole Root Rauwolfia Serpentina

Raudixin is Squibb Standardized Rauwolfia Serpentina Whole Root, an antihypertensive agent prepared from the powdered whole root of *Rauwolfia serpentina* Benth. It is standardized by pharmacognostic, chemical, and biological tests.

*Action:* Raudixin exerts the aggregate action of all the alkaloids contained in the whole *Rauwolfia serpentina* root. Thus, its therapeutic effect exceeds that of any single alkaloid from the root. For instance, in the rat, dog, and monkey, Raudixin has a hypotensive-tranquillizing action two to three times that accounted for by its reserpine content. In man, the antihypertensive effect of 250 mg. Raudixin is equivalent to that of 1 mg. reserpine, yet 250 mg. whole root contains only about 0.25 mg. reserpine by weight.

Raudixin has three basic pharmacologic actions, i.e., antihypertensive, tranquillizing and bradycardic. Generally, bradycardia is the first response to therapy as shown by a lowered pulse rate. The antihypertensive and tranquillizing effects develop more slowly over a period of one to three weeks and may continue for a week or more after the drug is discontinued.

In hypertension, Raudixin produces a gradual, sustained lowering of blood pressure, but does not significantly affect normal blood pressure. The gradual antihypertensive action gives patients time to adjust smoothly to new, lower, blood pressure levels without distressing episodes of dizziness or weakness due to sudden, sharp drops in pressure. Further, the sustained antihypertensive action is an added advantage for hypertensive patients who occasionally skip a dose; an accidentally omitted dose is not followed by a sudden, dangerous rise in blood pressure.

Due to its tranquillizing action, Raudixin is valuable in the management of anxiety and tension states and particularly effective in neurogenic hypertension, i.e., essential hypertension with the emotional component predominating. This tranquillizing effect affords relief of such common hypertensive symptoms as anxiety, tension, headache, insomnia and palpitations; patients generally experience sense of well-being without lethargy. The bradycardic effect of Raudixin reduces the work load of the heart, helping to increase cardiac efficiency. Although generally mild, the bradycardic effect may be marked in the hypertensive with tachycardia, in whom the drug may reduce the heart rate to normal.

*Advantages:*

* effective antihypertensive action
* gradual antihypertensive action which lets patients adjust smoothly to new, lower blood pressure levels
* sustained antihypertensive action which protects patients who occasionally skip a dose by accident
* complementary antihypertensive action when used with other antihypertensive agents
* effective tranquillization for management of anxiety and tension states and for helping relieve emotional aspects of hypertension

* bradycardia to increase cardiac efficiency
* few serious gastrointestinal side effects
* no habituation (tolerance not reported)
* long-term safety (has been given continuously for years)
* meticulous standardization for consistent, predictable results

*Indications:*

*In Hypertension.* Raudixin alone is frequently sufficient in mild to moderate hypertension. It is the antihypertensive agent of choice when the emotional component is the predominant factor. Many clinicians prefer its gradual, gentle action since hypertensive patients, particularly the elderly, do not tolerate sudden changes in blood pressure well.

When an additional antihypertensive effect is needed, combination therapy is recommended, such as that provided by Di-Raudixin® (Squibb Rauwolfia Serpentina Whole Root (Raudixin) and Hydroflumethiazide). Raudixin may also be used in conjunction with a suitable diuretic or other hypotensive agent, e.g., hydralazine, ganglionic blocking agents, or guanethidine.

*As a Tranquillizing Agent.* Raudixin is indicated in the management of anxiety and tension states and other conditions characterized by nervousness, irritability, excitability, and insomnia. The drug is of value in certain compulsive and other behaviour disorders. In addition, it is useful as adjunctive therapy in a number of disorders with emotional overlay, such as certain dermatoses, tension headache, some menopausal symptoms and chronic insomnia. The drug is also worthy of trial in the management of hyperirritable and hypertonic children, in the control of enuresis and in behaviour problems.

*Adverse Reactions and Precautions:* Rauwolfia preparations are known to cause diarrhoea, weight gain, nausea and vomiting, drowsiness, nasal stuffiness, reversible extrapyramidal tract symptoms, bizarre dreams, emotional depression and anxiety. Like any preparation containing Rauwolfia or its alkaloids, Raudixin should be administered with caution to patients with a history of depression or suicidal tendencies. Patients exhibiting signs of depression should be placed on lower dosage or the drug should be discontinued.

Patients on high dosage should be observed carefully at regular intervals to detect possible reactivation of peptic ulcer.

Since some patients receiving Rauwolfia preparations have experienced marked hypotension under surgical anaesthesia, it may be advisable to discontinue therapy for a period of about 2 weeks prior to elective surgery. Emergency surgery may be done by using anticholinergic or adrenergic drugs if necessary to prevent vagal circulatory responses; other supportive measures may be used as indicated.

Water retention with oedema in patients with hypertensive vascular disease occurs rarely, but it generally clears with cessation of therapy or with the administration of a diuretic agent such as Di-Ademil® (Squibb Hydroflumethiazide).

*Administration and Dosage:*

*Management of Hypertension.* Raudixin does not require the continual and often difficult adjustment of dosage common to other hypotensive agents. Adult patients may be started on a dose of 200 mg. daily, given as a single dose or divided and given morning and evening.

The full antihypertensive effect may not be seen for one to three weeks. Adjustments in dosage should be made after the full effect of the drug has occurred. Maintenance dosage may range from 50 to 300 mg. per day, given as a single dose or as two divided doses. Some patients on maintenance therapy require much smaller doses while others do better with larger doses. Dosage may be increased if there are no complaints of side effects and if the antihypertensive effect is insufficient. Dosage should be reduced if undesirable side effects appear. Raudixin is given continuously, not in interrupted courses of therapy. In contrast to other antihypertensive agents, frequent observation of blood pressure is not required, since postural syncope is not a problem.

This same dosage regimen is recommended when Raudixin is combined with other antihypertensive drugs. However, concomitant use with ganglionic blocking agents, hydralazine or guanethidine necessitates an immediate dosage reduction by at least 50% of the other more toxic agents, thus minimizing the incidence and severity of their side effects.

*Management of Emotional Disorders.* In adults, the anxious patient or the patient with physical symptoms complicated by emotional factors, dosage may start with 200 mg. daily, given as a single or divided dose. Dosage may be adjusted upward or downward, depending upon the degree of tranquillization achieved. In adjusting dosage, it is important to take into account the fact that results of therapy tend to appear slowly. Maintenance doses may vary from 50 to 300 mg. per day, given as a single dose or as two divided doses.

*Note:* Dosage for adolescents, children and the aged should be proportionately less than the usual adult dosage.

*Supply:* Coated tablets, 100 mg., bottles of 25 and 100.

## RECLOR®

**Capsules**

Squibb Chloramphenicol 250 mg. and Ascorbic Acid (Vitamin C) 250 mg.

## RECLOR® 500 mg.

**Capsules**

Squibb Chloramphenicol 500 mg. and Ascorbic Acid (Vitamin C) 250 mg.

Reclor is a combination of chloramphenicol and ascorbic acid. Each capsule of Reclor contains chloramphenicol 250 mg. and ascorbic acid 250 mg. Each Reclor 500 mg. capsule contains chloramphenicol 500 mg. and ascorbic acid 250 mg.

*Action:* Chloramphenicol is an antibiotic produced by the soil mould *Streptomyces venezuelae* and it can also be prepared synthetically. It inhibits the growth of a wide range of gram-positive and gram-negative bacteria, rickettsiae and viruses. Vitamin C is known to disappear from the blood of patients with fever more quickly than it does from the normal persons. The accelerated metabolism asso-

ciated with the elevated temperature is considered to be the cause of the increased utilization of this vitamin. This is particularly significant in human beings who cannot synthesize this vitamin in the body. Vitamin C is known to play the following roles in infections:

1. It assists in resistance of infection
2. It helps in the production of antibodies
3. It has a stimulative influence on phagocytic activity
4. It is necessary for many detoxification mechanisms

Vitamin C also helps in the healing of wounds. Vitamin C as contained in the formulation provides an adequate supply to counterbalance the depletion of vitamin C in infected and febrile states.

*Indications:* Reclor is the drug of choice in the treatment of typhoid fever and Haemophilus influenzae infection. Reclor is of value in typhus, Rocky Mountain spotted fever, lymphogranuloma venereum, primary atypical pneumonia, psittacosis, Salmonella and Shigella infections and bacillary urinary infections, especially when the causative organisms are resistant to the commonly used tetracycline group of broad spectrum antibiotics or other antibiotics.

*Advantages:* Reclor not only provides broad spectrum antibiotic activity of chloramphenicol but also provides ascorbic acid which is found highly beneficial during infective conditions and also for the healing processes.

*Dosage:* The suggested adult dose for chloramphenicol is 1.5 to 3 grammes per day in divided doses. In typhoid fever 3 grammes per day can be given in divided doses. This dose may be continued until the patient becomes afebrile. Thereafter the dosage can be reduced and that should be continued further for one or two weeks more. Longer treatment may be desirable in severe cases to decrease the incidence of relapse.

*Warning:* Blood dyscrasias have occurred after both short-term and prolonged therapy with chloramphenicol. Serious and even fatal dyscrasias (aplastic anaemia, hypoplastic anaemia, thrombocytopenia, granulocytopenia) are known to occur after the administration of chloramphenicol. Bearing in mind the possibility that such reactions may occur, chloramphenicol should be used only for serious infections caused by organisms which are susceptible to its antibacterial effects. Chloramphenicol should not be used when other less potentially dangerous agents will be effective, or in the treatment of trivial infections such as cold, influenza or viral infections of the throat or as a prophylactic.

*Precautions:* It is essential that adequate blood studies be made during the treatment with the drug. While blood studies may detect early peripheral blood changes such as leucopenia or granulocytopenia, before they become irreversible, such studies cannot be relied on to detect bone marrow depression, prior to development of aplastic anaemia.

*Supply:* Reclor Capsules 250 mg., bottles of 12 capsules.

Reclor Capsules 500 mg., bottles of 6 capsules.

*Expiration date* 24 months.

## RECLOR® SUSPENSION — Oral Suspension

Squibb Chloramphenicol Suspension

Reclor Suspension (Squibb Chloramphenicol Suspension) is a ready made flavoured aqueous suspension of chloramphenicol palmitate. Each 5 ml. of Reclor Suspension provides chloramphenicol palmitate equivalent to 125 mg. of chloramphenicol.

*Action:* Chloramphenicol is an antibiotic produced by the soil mould *Streptomyces venezuelae* and it can also be prepared synthetically. It inhibits the growth of a wide range of gram-positive and gram-negative bacteria, rickettsiae and viruses.

*Indications:* Reclor Suspension is the drug of choice in the treatment of typhoid fever and Haemophilus influenzae infection. Reclor Suspension is of value in typhus, Rocky Mountain spotted fever, lymphogranuloma venereum, primary atypical pneumonia, psittacosis, Salmonella and Shigella infections and bacillary urinary infections, especially when the causative organisms are resistant to the commonly used tetracycline group of broad spectrum antibiotics or other antibiotics.

*Warning:* Blood dyscrasias have occurred after both short-term and prolonged therapy with chloramphenicol. Serious and even fatal dyscrasias (aplastic anaemia, hypoplastic anaemia, thrombocytopenia, granulocytopenia) are known to occur after the administration of chloramphenicol. Bearing in mind the possibility that such reactions may occur, chloramphenicol should be used only for serious infections caused by organisms which are susceptible to its antibacterial effects. Chloramphenicol should not be used when other less potentially dangerous agents will be effective, or in the treatment of trivial infections such as cold, influenza or viral infections of the throat or as a prophylactic.

*Precautions:* It is essential that adequate blood studies be made during the treatment with the drug. While blood studies may detect early peripheral blood changes such as leucopenia or granulocytopenia, before they become irreversible, such studies cannot be relied on to detect bone marrow depression, prior to development of aplastic anaemia.

*Dosage:* The dose for children should be calculated as 25-50 mg. per Kg. of body weight per day and given in divided doses. Since neonates are unable to conjugate and excrete the antibiotic effectively, the dosage upto 25 mg. per Kg. of body weight per day in four equal doses at six-hour intervals usually produces and maintains adequate concentrations in blood and tissues to control most infections for which the drug is indicated. Increased dosage in infants demanded by severe infections may be given a dosage of 50 mg. per Kg. per day only during the acute stage of illness and the dosage should be reduced to 25 mg. per Kg. per day as soon as improvement occurs. Older children with severe infections may require a dosage upto 100 mg. per Kg. per day; however, it is recommended that the dosage be reduced to 50 mg. per Kg. per day as soon as possible.

*Supply:* Reclor Suspension is available in bottles of 60 ml. Each 5 ml. of suspension provides chloramphenicol palmitate equivalent to 125 mg. of chloramphenicol base.

*Expiration date* 18 months.

## RESTECLIN®

**Capsules**

Squibb Tetracycline Hydrochloride 250 mg. with
Ascorbic Acid (Vitamin C) 250 mg.

## RESTECLIN® 500 mg.

**Tablets**

Squibb Tetracycline Hydrochloride 500 mg. with
Ascorbic Acid (Vitamin C) 250 mg.

Resteclin Capsules contain 250 mg. crystalline tetracycline hydrochloride and 250 mg. ascorbic acid. Resteclin Tablets contain 500 mg. crystalline tetracycline hydrochloride and 250 mg. ascorbic acid. Although the chemical and physical properties as well as the antibacterial spectrum of tetracycline hydrochloride resemble those of oxytetracycline and chlortetracycline, tetracycline hydrochloride offers the advantage of greater stability in plasma and, on oral administration, there are fewer gastrointestinal side effects. In addition, tetracycline hydrochloride rapidly achieves effective blood and tissue concentrations.

*Action:* Tetracycline hydrochloride provides proven therapeutic effectiveness against infections caused by a broad spectrum of micro-organisms including both gram-positive and gram-negative bacteria, spirochaetes, certain rickettsiae, viruses of the lymphogranuloma-psittacosis-trachoma group, Eaton's agent and *Endamoeba histolytica*. Following oral administration, tetracycline hydrochloride is readily absorbed from the gastrointestinal tract with prompt establishment of fully effective blood concentrations. The antibiotic is rapidly diffused into various body fluids, including the cerebrospinal, peritoneal and pleural fluids, and the saliva. It appears to be mainly excreted in the urine, although some portions of the ingested drug are excreted unchanged in the faeces.

Vitamin C is known to disappear from the blood of patients with fever more quickly than it does from the normal persons. The accelerated metabolism associated with the elevated temperature is considered to be the cause of the increased utilization of this vitamin. This is particularly significant in the human beings, who cannot synthesize this vitamin in the body. Vitamin C is known to play the following roles in infections:

1. It assists in resistance of infection
2. It helps in the production of antibodies
3. It has a stimulative influence on phagocytic activity
4. It is necessary for many detoxification mechanisms

Vitamin C as contained in the formulation provides an adequate supply to counterbalance the depletion of vitamin C in infected and febrile states.

*Advantages:*

Tetracycline in Resteclin
* is effective against a wide variety of organisms
* is readily absorbed from the gastrointestinal tract
* rapidly diffuses into body fluids

and addition of

Vitamin C in Resteclin
* provides stimulating influence on phagocytic activity
* helps in the production of antibodies
* accelerates wound healing
* improves detoxification mechanism of the body

*Indications:* Resteclin is indicated for the many common infections including those of the respiratory, gastrointestinal and genitourinary systems which are amenable to tetracycline therapy.

Representative infections in which Resteclin may be used are:

*Pneumococcal Infections*
lobar pneumonia

*Streptococcal Infections*
cellulitis
bronchopneumonia
follicular tonsillitis
meningitis
otitis media
pharyngitis
scarlet fever
septic sore throat
tonsillitis
tracheobronchitis
urinary tract infections

*Staphylococcal Infections*
abscesses
acute bronchitis
furunculosis
impetigo
laryngotracheitis
ophthalmic infections
osteomyelitis
otitis media
pharyngitis
septicaemia
sinusitis
tracheobronchitis
urinary tract infections

*Neisseria Infections*
gonorrhoea
meningitis

*Proteus Infections* (due to tetracycline-sensitive strains)

*Escherichia coli Infections*
abscesses
peritonitis
urinary tract infections

*Shigella Infections*
bacillary dysentery

*Haemophilus Infections*
*Pertussis*

*Rickettsial Infections*
epidemic typhus
Rocky Mountain spotted fever

*Virus-like Infections*
lymphogranuloma
psittacosis
trachoma

*Intestinal Amoebic Infections*

*Acute Brucellosis* (in conjunction with streptomycin)

Resteclin is particularly valuable in the treatment of mixed infections due to susceptible organisms and in conditions in which the causal agent has not been specifically identified; for example, pneumonia, peritonitis, chronic bronchi-

ectasis, sinusitis, urinary tract infections, postpartum endometritis, puerperal mastitis, and pancreatitis. Resteclin is also recommended for mixed infections of the eye including conjunctivitis, corneal infection, periorbital infection, uveitis and some forms of blepharitis, and for such pyogenic dermatologic conditions as secondarily infected atopic dermatitis, sycosis and eczematous otitis externa. Resteclin is also useful in preoperative and postoperative prophylaxis.

*Dosage:* Dosage should be based on the tetracycline content: The suggested minimum adult dosage is 250 mg. four times daily. Higher dosages, such as 500 mg. four times daily, may be required for severe infections or for those infections which do not respond to the smaller dose. In general, the paediatric dosage should supply 20 to 40 mg. tetracycline per Kg. of body weight each day, in divided doses, depending on the type and severity of the infection.

Treatment of most common infections should generally continue for 24 to 48 hours after symptoms and fever subside. However, if used in the treatment of streptococcal infections, therapy should be continued for a full 10 days to guard against the risk of rheumatic fever or glomerulonephritis. Even more prolonged therapy is necessary for subacute bacterial endocarditis and may be required in certain staphylococcal infections.

*Side Effects:* Tetracycline hydrochloride is generally well tolerated. Undesirable side effects such as nausea, vomiting and diarrhoea are significantly less frequent with tetracycline hydrochloride than with the two analogues, oxytetracycline and chlortetracycline. If necessary, Resteclin may be given with cold milk or a light meal.

*Precautions:* As with any antibiotic preparation, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi (monilia). Constant observation of the patient is essential. Should superinfection occur, the drug should be discontinued and/or appropriate therapy instituted.

Tetracycline may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans. However, use of tetracycline during tooth development (i.e., last trimester of pregnancy, neonatal period and early childhood) may cause discoloration of the teeth (i.e., yellow-grey-brownish). This effect occurs mostly during long-term use of the drug but it has also been observed in usual short-treatment courses.

*Warning:* If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulation of the drug and possible liver toxicity. Under such conditions, lower than usual doses are indicated and if therapy is prolonged tetracycline serum level determinations may be advisable.

*Supply:* Resteclin Capsules 250 mg., vials of 4 capsules and nested packing of 25 vials of 4's. Resteclin Tablets 500 mg., vials of 2 tablets and nested packing of 25 vials of 2's.

*Expiration date* 24 months.

## RESTECLIN® INTRAMUSCULAR — Sterile Powder

Squibb Tetracycline Hydrochloride for
Intramuscular Use with Lidocaine (Xylocaine §)

Resteclin Intramuscular is available in powder form in vials providing 100 mg. crystalline tetracycline hydrochloride with 40 mg. lidocaine hydrochloride, buffered with 300 mg. ascorbic acid and 47 mg. magnesium chloride. Because lidocaine produces a more intensive and extensive anaesthetic effect, the preparation contains lidocaine (Xylocaine), rather than procaine.

Although the chemical and physical properties as well as the antibacterial spectrum resemble those of oxytetracycline and chlortetracycline, tetracycline hydrochloride offers the advantage of greater stability in plasma and fewer gastrointestinal side effects. In addition, it rapidly achieves fully effective blood and tissue levels.

*Advantages:*

* broad spectrum activity against both gram-positive and gram-negative bacteria as well as *Endamoeba histolytica* and certain rickettsiae and viruses
* particularly valuable in the treatment of mixed infections
* prompt absorption from site of injection
* rapid antibacterial levels in blood, cerebrospinal fluid and tissues
* prolonged antibacterial effect in urine
* greater stability in plasma than oxytetracycline or chlortetracycline
* minimal discomfort upon injection assured through the action of Xylocaine—the long acting local anaesthetic

*Indications:* Resteclin Intramuscular is intended for those patients unable or unwilling to take oral therapy. The parenteral form should be replaced by oral therapy as soon as the patient's condition permits.

It exhibits antimicrobial activity against a wide variety of gram-positive and gram-negative bacteria, rickettsiae, *Endamoeba histolytica*, and viruses of the lymphogranuloma-psittacosis-trachoma group.

Representative infections in which Resteclin Intramuscular may be used are:

*Pneumococcal Infections*
lobar pneumonia

*Streptococcal Infections*
cellulitis
bronchopneumonia
follicular tonsillitis
meningitis
otitis media
pharyngitis
scarlet fever
septic sore throat
tonsillitis
tracheobronchitis
urinary tract infections

§ 'Xylocaine' is a trade mark of Astra Pharmaceutical Products, Inc. for Lidocaine.

*Staphylococcal Infections*
abscesses
acute bronchitis
furunculosis
impetigo
laryngotracheitis
ophthalmic infections
osteomyelitis
otitis media
pharyngitis
septicaemia
sinusitis
tracheobronchitis
urinary tract infections

*Neisseria Infections*
gonorrhoea
meningitis

*Proteus Infections* (due to tetracycline-sensitive strains)

*Escherichia coli Infections*
abscesses
peritonitis
urinary tract infections

*Shigella Infections*
bacillary dysentery

*Haemophilus Infections*

*Pertussis*

*Rickettsial Infections*
epidemic typhus
Rocky Mountain spotted fever

*Virus-like Infections*
lymphogranuloma
psittacosis
trachoma

*Intestinal Amoebic Infections*

*Acute Brucellosis* (in conjunction with streptomycin)

Resteclin Intramuscular is particularly valuable in the treatment of mixed infections and in conditions in which the causal agent has not been specifically identified, for example, pneumonia, peritonitis, chronic bronchiectasis, sinusitis, urinary tract infections, postpartum endometritis, peurperal mastitis, and pancreatitis. The preparation is also recommended for mixed infections of the eye including conjunctivitis, corneal infections, periorbital infection, uveitis and some forms of blepharitis, and for such pyogenic dermatologic conditions as secondarily infected atopic dermatitis, sycosis and eczematous otitis externa. Resteclin Intramuscular is also useful in pre- and post-operative prophylaxis.

*Contraindications:* This drug is contraindicated in individuals with a history of tetracycline sensitivity.

*Warning:* If renal impairment exists, even usual oral or parenteral doses may lead to excessive systemic accumulation of the drug and possible liver toxicity. Under such conditions, lower than usual doses are indicated and if therapy is prolonged, tetracycline serum level determinations may be advisable.

Certain hypersensitive individuals may develop a photodynamic reaction precipitated by a direct exposure to natural or artificial sunlight during the use of this drug. This reaction is usually of the photoallergic type which may also be produced by other tetracycline derivatives. Individuals with a history of photosensitivity reactions should be instructed to avoid direct exposure to natural or artificial sunlight while under treatment with this or other tetracycline drugs, and treatment should be discontinued at first evidence of skin discomfort.

*Note:* Photosensitization reactions have occurred most frequently with demethylchlortetracycline, less with chlortetracycline, and very rarely with oxytetracycline and tetracycline hydrochloride.

*Precautions:* Therapy should be given under the constant supervision of a physician. The use of any broad spectrum antibiotic may result in overgrowth of non-susceptible organisms, particularly monilia. If new infections appear during therapy, appropriate measures should be taken. Tetracycline may form a stable calcium complex in any bone-forming tissue with no serious harmful effects reported thus far in humans. However, use of tetracycline during tooth development (i.e., last trimester of pregnancy, neonatal period and early childhood) may cause discoloration of the teeth (i.e., yellow-grey-brownish). This effect occurs mostly during long-term use of the drug but it has also been observed in usual short-treatment courses.

Increased intracranial pressure with bulging fontanels has been observed in infants taking therapeutic doses of tetracycline. Occurrence has been rare, and all signs and symptoms have disappeared rapidly upon cessation of treatment. In the treatment of gonorrhoea, patients with a suspected lesion of syphilis should have darkfield examinations before receiving tetracycline and monthly serologic tests for a minimum of three months.

The use of tetracycline in staphylococcal infections does not preclude the need for indicated surgical procedures.

*Administration:* The preparation should be administered by deep intramuscular injection following aspiration to be sure the needle is not in a vein. The preferred site is the upper outer quadrant of the buttock. Deposition in the subcutaneous tissues should be avoided; accidental injection into these tissues may cause pain and induration which can be alleviated by applying an ice bag.

*Directions for Reconstitution:* Add 2 ml. Sterile Water for Injection in the following manner: loosen the powder; hold the vial horizontally and rotate it while slowly directing the stream of diluent against the wall of the vial; shake the vial vigorously after the diluent has been added.

*Dosage: Adults:* Intramuscular administration of 200 to 300 mg. per day, given in divided doses of 100 mg. every 8 to 12 hours, is generally adequate for the treatment of susceptible infections of mild or moderate severity. In more severe infections or in those patients not responding to the above dosage schedule, 100 mg. every 4 or 6 hours may be given.

*Infants and Children:* Dosage for infants and children should be proportionately less than the adult dose, depending on the age, weight and severity of the condition being treated.

Therapy should be continued one or two days after signs and symptoms of the disease being treated have subsided. If a tetracycline preparation is used to treat haemolytic streptococcal infections, therapy should be continued for at least 10 days to guard against the risk of rheumatic fever or glomerulonephritis. Even more prolonged therapy is necessary for subacute bacterial endocarditis and for certain staphylococcal infections.

*Supply:* Resteclin Intramuscular, vials of 100 mg., boxes of 5 vials.

*Expiration date* 24 months at room temperature. After reconstitution, may be stored at room temperature, but should be used within 24 hours.

## RESTECLIN® INTRAVENOUS

**Sterile Powder**

Squibb Tetracycline Hydrochloride Crystalline
Buffered with Ascorbic Acid (Vitamin C) for Intravenous Use

Resteclin Intravenous is Squibb Tetracycline Hydrochloride for Injection. Although the chemical and physical properties as well as the antibacterial spectrum resemble those of oxytetracycline and chlortetracycline, tetracycline hydrochloride offers the advantage of greater stability in plasma and rapid achievement of effective blood and tissue concentrations.

Resteclin Intravenous is available in powder form in vials of 250 mg. and 500 mg. with vitamin C as a buffer.

*Rationale for Use:* Resteclin Intravenous is intended for those unable or unwilling to take oral Resteclin therapy. The parenteral form of Resteclin should be replaced by oral therapy as soon as the patient's condition permits.

*Indications:* Tetracycline hydrochloride has exhibited antimicrobial activity against a wide variety of gram-positive and gram-negative bacteria, rickettsiae, *Endamoeba histolytica*, and viruses of the lymphogranuloma-psittacosis-trachoma group. Resteclin Intravenous is indicated in the treatment of infections caused by susceptible organisms.

Representative infections in which Resteclin Intravenous may be used are:

*Pneumococcal Infections*
lobar pneumonia

*Streptococcal Infections*
cellulitis
bronchopneumonia
follicular tonsillitis
meningitis
otitis media
pharyngitis
scarlet fever
septic sore throat
tonsillitis
tracheobronchitis
urinary tract infections

*Staphylococcal Infections*
abscesses
acute bronchitis
furunculosis
impetigo
laryngotracheitis
ophthalmic infections
osteomyelitis
otitis media
pharyngitis
septicaemia
sinusitis
tracheobronchitis
urinary tract infections

*Neisseria Infections*
gonorrhoea
meningitis

*Proteus Infections* (due to tetracycline-sensitive strains)

*Escherichia coli Infections*
abscesses
peritonitis
urinary tract infections

*Shigella Infections*
bacillary dysentery

*Haemophilus Infections*

*Pertussis*

*Rickettsial Infections*
epidemic typhus
Rocky Mountain spotted fever

*Virus-like Infections*
lymphogranuloma
psittacosis
trachoma

*Intestinal Amoebic Infections*

*Acute Brucellosis* (in conjunction with streptomycin)

Resteclin Intravenous is particularly valuable in the treatment of mixed infections and in conditions in which the causal agent has not been specifically identified, for example, pneumonia, peritonitis, chronic bronchiectasis, sinusitis, urinary tract infections, postpartum endometritis, puerperal mastitis, and pancreatitis. Resteclin Intravenous is also recommended for mixed infections of the eye, including conjunctivitis, corneal infections, periorbital infection, uveitis and some forms of blepharitis, and for such pyogenic dermatologic conditions as secondarily infected atopic dermatitis, sycosis and eczematous otitis externa. Resteclin Intravenous is also useful in pre- and post-operative prophylaxis.

*Administration:* Administration by intravenous drip is the method of choice, although direct intravenous injection may be made, if necessary.

*For Intravenous Drip Therapy:* Resteclin Intravenous should be reconstituted with Sterile Water for Injection by adding 5 ml. or 10 ml. to the 250 mg. vial, and 10 ml. to the 500 mg. vial. The preferable concentration for intravenous drip is 0.1% or less (1 mg./ml.) which may be attained by further dilution of the solution with one of the standard intravenous solutions such as:

5% Dextrose Injection
Dextrose and Sodium Chloride Injection (Dextrose 5%)
Sodium Chloride Injection
Lactated Ringer's Injection

The usual rate of injection by intravenous drip is 5 to 10 ml. per minute.

*For Direct Intravenous Therapy:* Each 100 mg. Resteclin Intravenous should be dissolved in 10 ml. Sterile Water for Injection to make a 1% solution. The 1% solution may be administered directly by vein, allowing about 5 minutes for each 10 ml. (100 mg.) of the solution.

*Dosage: Adults:* The *average* adult dose for Resteclin Intravenous is 500 mg. every 12 hours. The *maximum* adult dose is 500 mg. intravenously every 6 hours. Duration of therapy should depend on the nature and severity of the infection. Therapy with Resteclin Intravenous should be continued 2 or 3 days after signs and symptoms of the disease being treated have subsided. Parenteral therapy with Resteclin Intravenous should be replaced by oral therapy as soon as the patient's condition permits.

If tetracycline is used to treat haemolytic streptococcal infections, therapy should be continued for at least 10 days to guard against the risk of rheumatic fever or glomerulonephritis. Even more prolonged therapy is necessary for subacute bacterial endocarditis and for certain staphylococcal infections.

*Precautions:* The usual precautions for intravenous therapy should be observed. As with other intravenously administered drugs, local inflammatory reactions at the injection site or thrombophlebitis may occur in some patients. Resteclin therapy should be given under the constant supervision of a physician.

The use of any broad spectrum antibiotic may result in overgrowth of non-susceptible organisms, particularly monilia. If new infections appear during therapy, appropriate measures should be taken. Intestinal moniliasis which may occur following oral administration of broad spectrum antibiotics can be pre-

vented or treated with Mycostatin (Squibb Nystatin) or Fungizone (Squibb Amphotericin B).

*Supply:* Resteclin Intravenous, vials of 250 mg. and 500 mg.

*Expiration date* 24 months at room temperature. After reconstitution, may be stored at room temperature, but should be used within 24 hours.

## RESTECLIN® OINTMENT — Ointment

Squibb Tetracycline Hydrochloride

Resteclin is Squibb Tetracycline Hydrochloride. It is an antibiotic of known structure obtained in the crystalline state. Resteclin Ointment is indicated for the topical treatment and prophylaxis of local infections due to a large variety of gram-positive and gram-negative micro-organisms. Resteclin Ointment is formulated in a new emollient and protective ointment base: Plastobase® (Squibb Plasticized Hydrocarbon Gel). Plastobase is odourless, colourless and non-irritating; it is easy to apply. Resteclin Ointment prepared with Plastobase does not stain the skin or clothing, and the patient readily accepts it. Each gramme of Resteclin Ointment provides 30 mg. tetracycline hydrochloride.

*Indications:* Resteclin Ointment is indicated in local infections sensitive to the antibiotic. It has been found effective in infections due to some gram-positive and gram-negative organisms as well as in various mixed bacterial infections. Resteclin Ointment can be used specifically in skin infections, including pyogenic infections, pyodermatitis, dermatitis pustulosa, minor infected wounds or abrasions and secondary infections accompanying minor burns. The ointment is also indicated in the prevention of local secondary infections of minor wounds and surgical interventions.

*Administration:* Resteclin Ointment is especially prepared for topical therapy. Resteclin Ointment should be applied to the skin two or three times a day until recovery is complete. The length of treatment varies according to the nature and severity of the infection to be treated. When crusts are present, these must be removed by wet compresses or water and soap before Resteclin Ointment is applied.

*Note:* When treating infections that can spread systemically, the topical administration of Resteclin should be supplemented by oral therapy.

*Tolerance:* Resteclin Ointment is well tolerated. In some individuals allergic reactions can occur. If so, administration of the ointment should be suspended and appropriate therapeutic measures adopted.

*Supply:* Tubes of 15 Gms.

*Expiration date* 36 months at room temperature.

## RESTECLIN® OPHTHALMIC OINTMENT — Ophthalmic Ointment

Squibb Tetracycline Hydrochloride

Resteclin is Squibb Tetracycline Hydrochloride, a crystalline antibiotic of known structure. Resteclin Ophthalmic Ointment is intended for topical application in the treatment of infections of the eye caused by a variety of gram-positive

and gram-negative organisms. Resteclin Ophthalmic Ointment is formulated in a new emollient, protective and non-irritating ointment base, Plastobase® (Squibb Plasticized Hydrocarbon Gel). Each gramme of Resteclin Ophthalmic Ointment provides 10 mg. crystalline tetracycline hydrochloride.

*Indications:* Resteclin Ophthalmic Ointment is indicated in the treatment of ocular infections caused by staphylococci, pneumococci, Haemophilus influenzae, Morax-Axenfeld diplobacillus, Friedlaender bacillus, Streptococci, Aerobacter aerogenes, Proteus vulgaris, Proteus morganii, Escherichia coli, Alcaligenes faecalis, Pseudomonas pyocyanea, and in the treatment of trachoma.

Viral or viral-like ocular infections responding to Resteclin Ophthalmic Ointment include follicular conjunctivitis, inclusion conjunctivitis and dendritic keratitis.

*Administration and Dosage:* Apply to affected eye every 2 hours or oftener as the condition and response indicate. Severe infections may require treatment for several days; in certain instances, oral adjuvant tetracycline may be required. Mild infections may respond in as little as 48 hours.

*Precaution:* Overgrowth of non-susceptible organisms may occur following use of antibiotics. Close observation, with appropriate measures when necessary, is required for all patients.

*Tolerance:* Resteclin Ophthalmic Ointment is well tolerated. Allergic reactions may occur in certain individuals. If such reactions are encountered, use of the ointment should be discontinued and appropriate therapy instituted.

*Supply:* Tubes of 3.6 Gms. with ophthalmic tip.

*Expiration date* 36 months at room temperature.

## RUBRAFERATE®

**Capsules**

Squibb Iron, Vitamin C, Vitamin $B_{12}$ and Folic Acid

Rubraferate is Squibb Vitamin $B_{12}$, Folic Acid, Iron and Vitamin C (Ascorbic Acid) for oral use.

Each Rubraferate Capsule provides:

| | | |
|---|---|---|
| Vitamin $B_{12}$ (as $B_{12}$ Activity Concentrate Oral Powder) | 4.17 | mcg. |
| Ferrous Sulphate Exsiccated (supplying 38 mg. Iron) | 0.13 | Gm. |
| Vitamin C (Ascorbic Acid) | 50 | mg. |
| Folic Acid | 0.28 | mg. |

*Indications:* Rubraferate may be used in the treatment of many of the common macrocytic anaemias, including nutritional macrocytic anaemia, tropical sprue and non-tropical sprue and the megaloblastic anaemias of infancy. Rubraferate is particularly indicated in the treatment of anaemias caused primarily by iron deficiency complicated by deficiencies of other nutrients. Rubraferate may also be useful in anaemias associated with dietary inadequacy commonly characterized by malaise and chronic fatigue.

*Note:* When the diagnosis of Addisonian pernicious anaemia has been confirmed, treatement with parenterally administered vitamin $B_{12}$ should be instituted.

*Dosage:* The recommended therapeutic dose is 2 Rubraferate Capsules three times daily or as prescribed by the physician. A smaller daily dose may be used for maintenance therapy, after blood values have reached normal levels. When on maintenance therapy, the patient should be watched carefully and a higher daily dose substituted if there is a clinical remission, or if the blood values decline.

When Rubraferate is given as a dietary supplement, the suggested dose is 1 capsule daily or as directed by the physician.

*Supply:* Bottles of 25 and 100 capsules.

*Note:* Keep bottle tightly closed. Avoid exposure to extreme heat and sunlight.

*Expiration date* 24 months.

## RUBRAGRAN®-HP

**Capsules**

Squibb High Potency Haematinic

Rubragran-HP is Squibb High Potency Haematinic combination for oral administration.

Each Rubragran-HP Capsule contains:

| | |
|---|---|
| Ferrous Fumarate | 300 mg. |
| Vitamin C | 100 mg. |
| Pyridoxine | 10 mg. |
| Folic Acid | 2.5 mg. |
| Vitamin $B_{12}$ | 50 mcg. |

*Action:* Nutritional deficiencies seldom occur in a single essential factor and the altered physiology induced by deficiency of one essential nutrient may increase the body's need for other nutrients. It is, therefore, desirable to provide five nutrients fundamental in normal red blood cell development. Rubragran-HP supplies all five factors in adequate amount for normal haemopoiesis.

Rubragran-HP supplies:

*Iron:* Essential constituent of haemoglobin molecule; fundamental in preventing and correcting hypochromia and microcytosis. Ferrous fumarate is regarded as the easily tolerated, well absorbed and adequately utilised form of oral iron medication.

*Vitamin C:* Necessary for haemopoiesis; aids the absorption and utilization of iron and plays a significant role in the maturation of red blood cells. Vitamin C deficiency can cause a normocytic or macrocytic anaemia which will not respond to liver extract or iron, but will respond to Vitamin C. Evidence exists to show that Vitamin C has a sparing action on available folic acid.

*Action:* Rubramin-H induces remission of pernicious anaemia like cyanocobalamin, but it is retained in the body in greater amounts and for longer periods than cyanocobalamin. Increased retention of Rubramin-H (hydroxocobalamin) is reflected in a corresponding decrease in urinary excretion. The blood level obtained with Rubramin-H after 5 hours is 4.1 times higher than that of Rubramin, after 24 hours it is 12.8 times higher and after 4 weeks it is 5.2 times higher, when both are administered intramuscularly in a dose of 1,000 mcg.

*Indications:* Rubramin-H is indicated for pernicious anaemia with or without neurologic complications. The preparation is also of value in the treatment of other macrocytic, megaloblastic anaemias where aetiology suggests malabsorption of vitamin $B_{12}$ such as anaemia following gastrectomy or associated with gastric carcinoma, macrocytic anaemia of pregnancy and the puerperium and the megaloblastic anaemias associated with such gastrointestinal disorders as tropical and non-tropical sprue. (In certain macrocytic anaemias, vitamin $B_{12}$ may fail to produce a satisfactory response, folic acid being indicated alone, or in combination with Rubramin-H.)

Higher doses of Rubramin-H may be of benefit in trigeminal neuralgia, diabetic neuritis, alcoholic neuritis, herpes zoster, and other neuropathies associated with diabetes, malnutrition and alcoholism where pain is a major component.

*Advantages:* Rubramin-H is capable in providing consistently higher, more prolonged blood serum levels. This fact is particularly important in the initial therapy of severe pernicious anaemia and other conditions involving serious depletion of vitamin $B_{12}$, in which prompt replacement of body stores of vitamin is essential.

Adequate parenteral doses of Rubramin-H prevent or alleviate the neurological complications of pernicious anaemia, particularly subacute combined system disease. However, as is true of liver extract therapy, long-standing neurologic involvement may have progressed to the stage where damage is largely irreversible despite intensive vitamin $B_{12}$ therapy.

*Dosage:* The presently recommended dosage requirements for vitamin $B_{12}$ vary with the individual patient, and with the condition being treated. For uncomplicated pernicious anaemia, the suggested initial dose of Rubramin-H is 15 mcg. intramuscularly once or twice a week until normal haemoglobin levels are obtained. In severe cases of pernicious anaemia larger intramuscular doses, as high as 100 mcg. daily, may be required, particularly when neurological manifestations are present.

When remission occurs, maintenance dosage should be determined individually on the basis of red blood cell count. Intramuscular maintenance doses as low as 15 mcg. every other week, or 100 mcg. monthly or every other month, are generally sufficient to maintain blood values.

In sprue, 15 to 30 mcg. intramuscularly once or twice per week is generally sufficient to induce remission. Thereafter, as low as 15 mcg. may be required once per week to prevent relapse.

In nutritional macrocytic anaemia, a single initial intramuscular dose of 15 mcg. usually produces a favourable response. The suggested dose may be repeated every two weeks to prevent relapse. Concomitant therapy with folic acid may be required. For the treatment of neuritis and other neuropathies high dosage of 500 to 1,000 mcg. may be given at weekly intervals.

*Side Effects:* Very few reactions have been observed following parenteral administration. No toxic or cumulative effects have been reported following massive doses of vitamin $B_{12}$. Evidence indicates that patients unable to tolerate liver extracts may receive vitamin $B_{12}$ without untoward effect.

*Supply:* 500 mcg./ml. and 1,000 mcg./ml., vials of 5 ml.

*Expiration date* 36 months.

## RUBRAPLEX®

**Elixir**

Squibb Iron, B Complex and $B_{12}$ Vitamins Elixir

Rubraplex is Squibb Iron, B Complex and $B_{12}$ Vitamins Elixir. It supplies two important blood building factors as well as vitamins of the B Complex group. Rubraplex is a pleasant tasting, fruit-flavoured elixir which may be taken directly from the spoon, or mixed with a small amount of water, fruit juice or milk. Its excellent palatability makes Rubraplex particularly useful in patients who object to or are unable to take capsules or tablets.

Each 5 ml. (approximately 1 teaspoonful) of Rubraplex provides:

| | |
|---|---|
| Elemental Iron (as Ferric Ammonium Citrate and Colloidal Iron) | 38.0 mg. |
| Vitamin $B_{12}$ (Cyanocobalamin) | 4.0 mcg. |
| Vitamin $B_1$ (Thiamine Mononitrate) | 1.0 mg. |
| Vitamin $B_2$ (Riboflavine-5-Phosphate-Sodium) | 1.0 mg. |
| Vitamin $B_6$ (Pyridoxine Hydrochloride) | 0.5 mg. |
| d-Panthenol | 1.5 mg. |
| Niacinamide | 5.0 mg. |

Alcohol content: 12% by volume

*Indications:* Rubraplex is indicated in the treatment of anaemias due to nutritional deficiency. By virtue of its iron content, Rubraplex is particularly useful in the management of iron-deficiency anaemias. Specifically, Rubraplex is useful in the treatment of nutritional macrocytic anaemia and in the iron-deficiency anaemias of infancy, childhood and puberty, as well as in anaemias of women from menarche to menopause. The preparation is also of value in the treatment of anaemias attending convalescence. The B Complex vitamin content of Rubraplex makes the preparation suitable for the treatment of mild deficiencies of these vitamins.

Rubraplex may also be employed for the promotion of growth in infants and children.

*Rubraplex is not intended for the treatment of pernicious anaemia.*

*Advantages:*

* replenishes B Complex and $B_{12}$ vitamin reserves essential for all body tissues, including blood
* regenerates blood by supplying elemental iron
* restores physical well-being of patients in any age group

*Dosage: Treatment of Anaemia:* Dosage requirements for Rubraplex, like those of other anti-anaemia preparations, vary with the individual patients and the condition being treated. The average dose of Rubraplex for adults and children is 2 teaspoonfuls (10 ml.) three times daily. When remission occurs, a maintenance dose of 1 teaspoonful (5 ml.) three times daily is suggested. Patients on maintenance therapy should be watched carefully and larger doses of Rubraplex should be resumed if clinical regression occurs or blood values decline.

*Treatment of Mild B Complex Deficiencies:* The suggested dose for Rubraplex is 1 teaspoonful (5 ml.) three times daily. This dosage regimen may be used in adults and children.

*For Promotion of Growth:*

| | |
|---|---|
| Infants under 2 years of age | : The minimum dose is 1 teaspoonful (5 ml.) of Rubraplex three times daily. |
| Children 2 years of age or older | : The minimum dose is 2 teaspoonfuls (10 ml.) three times daily. |

*Administration:* Rubraplex is a pleasant tasting preparation and may be given directly from the spoon. However, if preferred, the preparation may be mixed with a small amount of water, fruit juice or milk.

*Supply:* Rubraplex is available in bottles of 120 ml., 240 ml. and 480 ml.

*Note:* Bottles of Rubraplex should be kept tightly closed and stored in a cool place. Exposure to sunlight should be avoided.

*Expiration date* 18 months.

## RUBRAPLEX® INJECTION — Parenteral Solution

Squibb Vitamin B Complex Injection

Rubraplex Injection, Squibb Vitamin B Complex Injection for intramuscular use, contains six important physiologically and therapeutically useful members of the B Complex vitamins. Rubraplex Injection formula is based on the recommendations of the National Formulary of India.

Each ml. Rubraplex Injection supplies:

| | |
|---|---|
| Vitamin $B_{12}$ (Cyanocobalamin) | 10 mcg. |
| Vitamin $B_1$ (Thiamine Hydrochloride) | 15 mg. |
| Vitamin $B_2$ (Riboflavine) | 2 mg. |
| Niacinamide | 100 mg. |
| Vitamin $B_6$ (Pyridoxine Hydrochloride) | 5 mg. |
| Panthenol | 5 mg. |

*Indications:* Rubraplex Injection contains all the major factors of vitamin B Complex in adequate amounts; it is useful for the vitamin B Complex deficiency states met with in clinical practice. Deficiency of a single factor of B Complex is relatively rare without a latent deficiency of other B Complex factors also. Hence Rubraplex Injection is indicated for the treatment of vitamin B Complex deficiency symptoms. These symptoms can be manifested as glossitis, stomatitis, ulcers of the mucous membranes of mouth, cheilosis, conjunctivitis, photophobia, epiphora, scleral injection, vomiting, anorexia, diarrhoea, neuritis, paraesthesias, tenderness of calf muscles, weakness, fatigue, vague neuritic pain, pellagrous dermatitis, burning foot syndrome, etc. It is also useful for debility during convalescence, vitamin B Complex deficiency due to broad spectrum antibiotic therapy, chronic debilitating diseases and diabetes mellitus.

Administration of Rubraplex Injection provides for the increased vitamin requirements accompanying alcoholism, thyrotoxicosis, serious illness or tissue damage caused by injury, burns, excessive radiation or surgery. Post-operatively, Rubraplex Injection therapy is recommended in the presence of anorexia or vomiting, particularly for patients receiving infusions of saline or glucose as such infusions may cause rapid depletion of water-soluble vitamins by increasing their rate of urinary excretion. Moreoever, many of the B Complex vitamins form enzymes essential for the oxidation of glucose and infusions of glucose solutions may deplete tissue stores of B vitamins. To compensate for this loss adequate amounts of these vitamins should be administered along with the infusion solutions. Since B vitamins are also concerned with protein and amino acid metabolism, liberal quantities of the vitamin B Complex should be given to patients receiving amino acid or protein preparations parenterally.

Rubraplex Injection is specially indicated in severe B Complex deficiencies, particularly in patients who cannot tolerate oral medication or in whom there is evidence of poor gastrointestinal absorption.

*Dosage:* One ml. intramuscularly, once or twice a day as may be decided by the physician.

*Supply:* Vials of 10 ml.

*Expiration date* 12 months. Store in a cold place, below 15°C.

## RUBRATON® Elixir

Squibb Iron-$B_{12}$-Folic Acid Elixir

Rubraton combines three fundamental blood-building factors in an exceptionally pleasant tasting elixir.

Each teaspoonful (5 ml.) of Rubraton contains:

| | |
|---|---|
| Elemental Iron (as Ferric Ammonium Citrate 0.22 Gm.) | 38 mg. |
| Vitamin $B_{12}$ | 4.17 mcg. |
| Folic Acid | 0.28 mg. |

Alcohol content: 12% by volume

*Indications:* Rubraton may be used for therapy in nutritional macrocytic anaemia, the megaloblastic anaemia of infancy, and in sprue. When iron deficiency is complicated by deficiencies of other nutrients, Rubraton is also indicated. It may be especially useful in anaemias which are difficult to classify and treat.

Therefore, Rubraton may be useful in the anaemias attending convalescence, the microcytic and normocytic anaemias of pregnancy, the anaemias of chronic bleeding and the iron-deficiency anaemias of infancy, childhood and puberty. In addition, Rubraton may be used experimentally for the promotion of growth in children. It is also useful in patients who object to capsules or tablets. *Rubraton is not intended for the treatment of pernicious anaemia.*

*Advantages:* Because of its contents of folic acid and vitamin $B_{12}$, Rubraton offers a pleasant, oral method for treating those anaemias, other than pernicious anaemia, characterized by megaloblastic arrest of the bone marrow. In addition, its iron content makes Rubraton specific in iron deficiency. Because it is a liquid, Rubraton offers better absorption of its constituents.

*Dosage:* In treating any anaemia it is probably best to administer an excess of haematogenic essentials. Hence, in the average case, therapy should be started with 2 teaspoonfuls of Rubraton t.i.d. Each dose should be taken in half a glass of water, milk or fruit juice. When indicated by clinical and haematologic response, the dose may be lowered to 1 teaspoonful t.i.d. When on maintenance therapy the patient should be carefully watched and a higher dose substituted if there appears to be a clinical regression, or if the blood values decline.

*Supply:* Bottles of 120 ml., 240 ml. and 480 ml.

*Note:* Keep tightly closed. Avoid exposure to sunlight.

*Expiration date* 18 months.

## RUBRATON® PEDIATRIC

**Elixir**

Squibb Iron-$B_{12}$-Folic Acid Elixir

Rubraton Pediatric is a good-tasting liquid supplying therapeutic amounts of three essential blood-building factors.

Each teaspoonful (5 ml.) Rubraton Pediatric contains:

| | |
|---|---|
| Elemental Iron (as Ferric Ammonium Citrate 0.22 Gm.) | 38 mg. |
| Vitamin $B_{12}$ | 4.17 mcg. |
| Folic Acid | 0.28 mg. |

Alcohol content: 5% by volume

*Indications:* Rubraton Pediatric combats anaemia (except pernicious anaemia) due to nutritional deficiencies in children. Rubraton supplies three important blood-building factors in therapeutically effective amounts, in a formulation acceptable in taste to the most exacting child.

Rubraton Pediatric is indicated for the treatment of anaemia (except pernicious anaemia) due to nutritional deficiencies in infants and children: Rubraton Pediatric has been used to promote growth in children.

*Administration:* Rubraton Pediatric may be taken directly from a spoon, or mixed with a small amount of water, fruit juice or milk.

*Dosage:* Children under 2 years—1 teaspoonful, three times daily.
Children 2 years and over—2 teaspoonfuls, three times daily.
Maintenance therapy—1 teaspoonful, three times daily.

*Supply:* Bottles of 60 ml.

*Note:* Keep tightly closed. Avoid exposure to sunlight.

*Expiration date* 18 months.

## SIQUIL®

**Tablets, Parenteral Solution**

Squibb Trifluprομazine Hydrochloride

Siquil, Squibb Trifluprομazine Hydrochloride is a highly potent phenothiazine derivative, chemically designated as 10-(3-dimethylaminopropyl)-2-(trifluoromethyl) phenothiazine hydrochloride. Siquil is available for oral, and parenteral administration. Oral and parenteral Siquil are indicated in the control of nausea and vomiting, as pre- and post-operative sedative agents, in obstetrics and in the management of anxiety and tension states. Oral and parenteral Siquil are also of value in the treatments of psychiatric disorders and of alcoholism. For oral use, Siquil is supplied as press-coated tablets. For parenteral administration, Siquil is available in ampoules and multiple dose vials.

*Action:* Siquil was synthesized and developed in the laboratories of The Squibb Institute for Medical Research. Modification of the phenothiazine structure as achieved in Siquil has resulted in a potentiation of beneficial pharmacologic properties with a concomitant reduction and attenuation of unwanted physiologic effects. Clinical appraisal has demonstrated that Siquil is at least twice as potent as chlorpromazine in controlling psychotic manifestations; in animal studies, Siquil exhibited a three to five fold increase in activity when compared with chlorpromazine. In clinical trials Siquil has shown a unique ability to control psychomotor agitation without producing marked sedation. These studies have revealed that sedation is not a necessary requisite in achieving pharmacologic benefits on psychotic symptoms such as agitation, delusions, hallucinations or delirium. Thus trifluprομazine does not put the patient into a state of lethargy and apathy, but, rather, allows the patient to be approached for training purposes and eventual rehabilitation. Investigation of the clinical effectiveness of trifluprομazine as an anti-emetic agent has shown the compound to be at least 5 times as potent as chlorpromazine in arresting nausea and vomiting.

The site and mode of action of phenothiazine derivatives including trifluprομazine are largely a matter of speculation. Experimental and clinical studies suggest that these compounds act on the hypothalamus. These drugs are believed to depress various components of the mesodiencephalic activating system which is involved in the control of basal metabolism and body temperature, wakefulness, vasomotor tone, emesis and hormonal balance. In addition, the drugs exert a peripheral autonomic effect. Like other phenothiazines, trifluprομazine prolongs and intensifies the action of many central nervous system depressants such as barbiturates, narcotics, and anaesthetics.

*Advantages:*

* increased potency without increased toxicity
* may be administered orally, intramuscularly or intravenously—well-tolerated by all routes of administration
* useful in children as well as adults
* tranquillizes the patient without marked sedation
* usually has no significant effect on blood pressure after oral administration
* relieves anxiety and tension with a minimum of unpleasant side effects
* is a superior anti-emetic agent, preventing or correcting emesis resulting from any of numerous causes
* provides extraordinary benefits when used prior to general anaesthesia since trifluprομazine does not interfere with respiration
* used adjunctively in the immediate post-anaesthetic period prevents or corrects "emergence delirium"
* as an adjunct to obstetrical analgesia potentiates the analgesic action of narcotics and sedatives and increases the tolerance to pain
* allays the distress of the post-alcoholic state
* favourably modifies aggressive and hostile psychotic behaviour, diminishes or dispels hallucinations and delirium, and restores or increases the accessibility of the patient to other forms of therapy
* is a versatile phenothiazine derivative

*Indications:*

### Nausea and Vomiting

Parenteral and oral Siquil are indicated in the control and prevention of nausea and vomiting associated with a variety of clinical disorders. Specifically, Siquil is useful in the control and prevention of nausea and vomiting associated with such clinical disorders as certain diseases, acute infections, certain neurological procedures such as encephalography and ventriculography, certain drugs, radiation therapy, and nitrogen-mustard therapy. The drug is of particular value for prophylaxis and therapy of nausea and vomiting of early pregnancy, up to and including the 12th week, as well as hyperemesis gravidarum, and for the control of post-operative emesis.

### Obstetrics

As an adjunct to narcotics and general anaesthetics during the first and second stages of labour, the administration of Siquil has a three-fold purpose: It provides a calming and sedative effect; it intensifies the action of narcotics and anaesthetics, so that dosage of these drugs can be greatly reduced; and it appreciably lowers the incidence of vomiting. No apparent effects on the new-born have been encountered following the use of trifluprómazine.

### Pre- and Post-operative Tranquillization

Parenteral Siquil has been used with great success preoperatively, particularly in combination with local anaesthesia. It is also well suited for use prior to general anaesthesia since it does not interfere with respiration. Moreover, its potentiating effect on general anaesthetics allows a reduction in the dosage of these agents. Although trifluprómazine has been used prior to spinal anaesthesia without any untoward effects, it is generally not recommended when spinal anaesthesia is contemplated.

### Alcoholism

Trifluprómazine has been of great value in the alleviation of restlessness, anxiety, insomnia and other emotional side effects commonly accompanying the withdrawal of alcohol.

### Anxiety and Tension

The ataractic effects of trifluprómazine are beneficial in the treatment of functional complaints arising from anxiety and tension, and in the alleviation of apprehension associated with such conditions as neurodermatitis, arthritis, and cardiovascular disease.

### Mental Disorders

Because of its highly potent behaviour modifying properties, the drug is useful in the management of psychomotor agitation associated with various acute and chronic psychoses including schizophrenia, mania, depression, delirium, senile psychoses, and psychoses due to organic brain disease or mental deficiency. Trifluprómazine may be used with appropriate caution in mental disorders associated with epilepsy.

Behavioural Problems in Children

Siquil is indicated in the management of primary behavioural problems in children.

*Contraindications:* Phenothiazine derivatives are contraindicated in patients with suspected or established subcortical brain damage, with or without hypothalamic damage, since a hyperthermic reaction with temperatures in excess of 104°F. has been reported to occur, sometimes as late as 14 to 16 hours after drug administration. Total body ice-packing is recommended for such a reaction; antipyretics may also be useful.

Because trifluprornazine may induce drowsiness in some patients, driving a motor vehicle or operating machinery while under trifluprornazine therapy is not recommended.

Phenothiazine compounds should not be used in patients receiving large doses of hypnotics, and should be used with caution in patients with a history of convulsive disorders, since grand mal-convulsions have been known to occur.

Patients with special medical disorders such as mitral insufficiency or pheochromocytoma and patients who have exhibited idiosyncrasy to other centrally-acting drugs may experience severe reactions to phenothiazine compounds.

*Adverse Reactions and Precautions:* The most frequently reported side effects associated with phenothiazine administration are reversible extrapyramidal symptoms including Parkinsonism, dystonia, dyskinesia, akathisia, oculogyric crises, opisthotonos, and hyper-reflexia. Although these reactions may be alarming, all are reversible and disappear if dosage is lowered or therapy is temporarily discontinued. More rapid reversal may be achieved by administration of anti-Parkinsonian drugs or intravenous Caffeine and Sodium Benzoate Injection.

Skin disorders such as itching, erythema, urticaria, and even exfoliative dermatitis have occurred with phenothiazine compounds. Photosensitivity, manifested as an erythematous macular eruption in sun-exposed areas, has been reported.

The possibility of anaphylactoid reactions occurring in some patients should be borne in mind.

Oral administration of trifluprornazine has produced dissociation of the cerebrospinal fluid protein pattern. A severe hypertensive reaction following 25 mg. of the drug was reported in one patient. Reactivation of psychotic processes or induction of a catatonic-like state may occur.

Drowsiness or lethargy, if they appear, may necessitate a reduction in dosage. Peripheral oedema, endocrine disturbances such as abnormal lactation, and autonomic reactions including nausea, dry mouth, headache, and constipation may occur. Autonomic effects can usually be controlled by reducing or temporarily discontinuing dosage.

Hypotension appears to be a particular problem in patients with pheochromocytoma or mitral insufficiency. If severe hypotension should occur, supportive

measures including the use of intravenous vasopressor drugs should be instituted immediately. Levarterenol Bitartrate Injection is the most suitable drug for this purpose: *epinephrine should not be used* since phenothiazine derivatives have been found to reverse its action, resulting in a further lowering of blood pressure. Patients on trifluprómazine therapy who are undergoing surgery should be watched carefully for possible hypotensive phenomena. Moreover, it should be remembered that dosages of anaesthetics and central nervous system depressants should be reduced.

As with other phenothiazines, potentiation of central nervous system depressants (opiates, analgesics, anti-histamines, barbiturates, alcohol), and of atropine occurs with trifluprómazine.

Liver damage as manifested by jaundice or biliary stasis may be encountered. Blood dyscrasias including leucopenia, agranulocytosis, thrombocytopenic purpura, eosinophilia, and pancytopenia, may occur in some patients. For this reason, routine blood counts are advisable during therapy. The patient should be observed for any soreness of the mouth, gums, or throat or any symptoms of upper respiratory infection. If these symptoms occur and confirmatory leucocyte count indicates cellular depression, therapy should be discontinued and other appropriate measures should be instituted immediately.

The following have never been reported with trifluprómazine, although they have occurred with other phenothiazine derivatives: Hypotension severe enough to cause fatal cardiac arrest, cerebral oedema, potentiation of phosphorus insecticides, eczema, asthma, laryngeal oedema, angioneurotic oedema, and pigmentary retinopathy.

*Caution:* The use of phenothiazines as a class is associated with different degrees of drowsiness. It is worthwhile to remember that engine crews, vehicle drivers and workers in workshops with fast moving parts, are advised not to use these drugs while on duty unless recommended and approved by the physician attending on them.

*Administration and Dosage:*

*Caution:* The parenteral administration of trifluprómazine may sometimes cause postural hypotension; to preclude its occurrence, patients should be kept under close clinical supervision, in a recumbent position if necessary. If severe shock is encountered, supportive measures should include intravenous vasopressor drugs such as Levarterenol Bitartrate Injection (Levophed); *epinephrine should not be used.*

NAUSEA AND VOMITING

Parenterally, adult dosage may range from 1 to 3 mg. intravenously or 5 to 10 mg. intramuscularly, for prophylaxis as well as for treatment. Dosage may be repeated after 4 hours, if necessary. Oral prophylactic dosage may range from 20 to 30 mg. daily. For elderly or debilitated patients an intramuscular dose of 2.5 mg. is suggested. For children the recommended dosage is 0.2 mg./Kg. (1/10 mg./lb.) up to a maximum total daily dose of 10 mg. divided into 3 doses orally, or a range of 0.2 to 0.25 mg./Kg. (1/10 to 1/8 mg./lb.) up to a maximum

total daily dose of 10 mg. intramuscularly. The drug should not be administered to children under 2½ years of age and is not recommended for intravenous use in children.

*For the Nausea and Vomiting of Early Pregnancy:* The suggested dosage is 10 mg. orally, given before breakfast or at bedtime. If required, 20 mg. daily may be given in divided doses before breakfast and at bedtime.

### Obstetrics

*First stage of labour:* 15 mg. intramuscularly plus one-half (½) the usual dose of a narcotic. Dosage may be repeated every 4 hours, as indicated. In primiparas, trifluprómazine should be given when the dilatation of the cervix is 3 cm. and pains are well established. In multiparas, dilatation of the cervix should be 5 cm. before the drug is given.

*Second stage of labour:* 8 mg. intravenously before anaesthesia is started. The amount of general anaesthesia required is generally greatly reduced when trifluprómazine is given. Premedication with one of the belladonna drugs is suggested.

### Pre- and Post-operative Tranquillization

*Intravenous:* 1 to 3 mg. as an initial adult dose; if necessary, an additional dose of one-fourth (¼) of the amount of the initial dose may be given as soon as desired.

*Intramuscular:* 5 to 10 mg. as an average initial adult dose; if required, a second injection may be given, but total doses of 20 mg. should not be exceeded. For elderly or debilitated patients an intramuscular dose of 2.5 mg. is suggested. For children, an intramuscular dosage regimen of 1 mg. per year of age up to 10 mg. is suggested. Some clinicians have employed the intravenous route of administration with great success, using a single dose of 2 to 3 mg. for children 7 to 14 years of age, and 1 to 2 mg. intravenously for those under 7 years of age. Generally drugs like trifluprómazine are not required for routine use in children under 2½ years of age.

### Alcoholism

For severely agitated patients, an initial intramuscular dose of 20 to 40 mg. is recommended, repeated, if necessary, in one or two hours. Thereafter, oral therapy should be instituted in a range of 10 to 25 mg. or more three times per day, depending on individual response.

### Anxiety and Tension

A daily oral dosage schedule of 20 to 50 mg. ranging, if required, up to 80 mg. in two divided doses has generally been adequate.

MENTAL DISORDERS AND BEHAVIOURAL PROBLEMS

*Institutionalized Adult Patients:*

Optimum dosage levels must be determined individually for each patient. The suggested starting dose for oral therapy is 100 to 150 mg. daily. After treatment is instituted, the daily dosage should be adjusted until the desired clinical effect is obtained. Continued treatment is necessary to achieve maximum therapeutic benefits. In some patients, optimum clinical improvement may occur only after prolonged treatment. When symptoms are controlled, dosage can generally be reduced gradually to maintenance levels.

The suggested intramuscular dose is 60 to 150 mg. daily. In clinical experience to date, total daily doses of 150 mg. have been well tolerated. Daily doses larger than 150 mg. should be exceeded with great caution.

*Non-institutionalized Adult Patients:*

Patients with severe mental disorders should receive the same regimen as outlined for institutionalized patients.

Patients on *maintenance therapy* following institutional care are generally benefited by daily oral doses of 30 to 150 mg.

*Children:*

As in adult therapy, optimum dosage levels must be determined individually for each patient. An oral dosage schedule of 30 mg. per day ranging, if required, up to 150 mg. daily in divided doses has generally been adequate. For maintenance therapy, dosage should be increased or decreased to meet individual requirements. When intramuscular use is indicated in children, the usual range has been 0.2 to 0.25 mg./Kg. of body weight (1/10 to 1/8 mg. per lb.).

*Senile Psychoses (Including Arteriosclerotic States):*

Initial dosage—10 mg. orally two to three times daily, adjusted to the response of the patient.

*Supply:* Tablets: 10 mg., boxes of 100 (10 strips of 10's).
25 mg., bottles of 25 and 250.

Injections: 3 mg./ml. and 10 mg./ml., 1 ml. ampoules in boxes of 5; 10 mg./ml., 10 ml. vials and 20 mg./ml., 5 ml. vials.

*Note:* Solutions of Siquil should be protected against exposure to light. The preparation may become somewhat discoloured if exposed to light, but this does not indicate any change which would prevent its use. However, when definite colour changes occur as a result of improper storage, the preparation should not be used. Store in a cool place.

## SPECTROCIN® OINTMENT — Ointment

Squibb Neomycin Sulphate-Gramicidin Ointment

Spectrocin Ointment is a general purpose antibiotic ointment of high quality. Each gramme of Spectrocin Ointment contains neomycin sulphate equivalent to 2.5 mg. neomycin base and 0.25 mg. gramicidin in Plastobase® (Squibb Plasticized Hydrocarbon Gel), a polyethylene and mineral oil gel base.

*Action:* Most of the organisms responsible for superficial bacterial infections are highly susceptible to neomycin; those which are resistant or only slightly susceptible to neomycin are usually susceptible to gramicidin. If topical use of an antibiotic causes sensitization, subsequent systemic use in that patient may be hazardous. Neomycin is rarely administered systemically, and gramicidin never. Therefore, even if sensitization to Spectrocin should occur, the patient need not be denied the use of valuable antibiotics that are generally used orally or parenterally for serious disorders.

*Advantages:* The plasticized hydrocarbon gel used in Spectrocin Ointment provides fast, regular and thorough release of medicaments and uniform dispersion of medicaments even at elevated temperatures.

Consistently soft, Spectrocin Ointment is easily applied to the skin and is *nonrunning* at body temperature. It imparts a velvety feel to the skin and can be readily removed. Spectrocin may be used for patients sensitive to other antibiotics.

*Indications:* Spectrocin Ointment is indicated to help in the prevention of superficial infections of the skin such as occur in minor burns, cuts, scratches or abrasions.

*Precautions:* In case of deep or punctured wounds or serious burns or conditions of the wounds indicate redness, irritation or swelling or pain persists or increases or infection occurs, please substitute alternate specific suitable ointment.

*Administration and Dosage:* Apply liberally to affected area two or three times daily or as directed by physician.

*Supply:* Tubes of 15 Gms.

*Expiration date* 36 months.

## SPECTROCIN® OPHTHALMIC OINTMENT — Ophthalmic Ointment

Squibb Neomycin Sulphate-Gramicidin Ophthalmic Ointment

Spectrocin Ophthalmic Ointment (neomycin sulphate-gramicidin ophthalmic ointment) is a smooth, white ointment containing neomycin sulphate equivalent to 2.5 mg. neomycin base and 0.25 mg. gramicidin in each gramme of Plastobase® (Squibb Plasticized Hydrocarbon Gel), a polyethylene and mineral oil gel base.

*Action:* The antibacterial spectrum of neomycin and gramicidin includes gram-positive and gram-negative organisms responsible for many bacterial infections of the eye. Most organisms causing these infections are highly susceptible to neomycin; those which are resistant or only slightly susceptible to neomycin are usually susceptible to gramicidin.

Hypersensitivity reactions to the topical application of neomycin or gramicidin are exceedingly rare. However, even if sensitivity to these agents should occur, it does not pose a problem in subsequent systemic therapy for the patient, since these antibiotics are rarely administered systemically. Certain other valuable antibiotics that are commonly given orally or parenterally for serious disorders can thus be reserved for such use.

*Advantages:* Spectrocin Ophthalmic Ointment is easily applied to the eyelid or conjunctiva, spreads smoothly, and does not melt at body temperature. It may be conveniently removed from the eyelid or conjunctiva since it is readily absorbed by cloth or cleansing tissue.

*Indications:* Spectrocin Ophthalmic Ointment is indicated for external use in superficial bacterial infections of the eyelids and lid margins, blepharitis due to bacterial infection, hordeolum, superficial bacterial infection of the conjunctiva and cornea, and as prophylaxis after extraction of foreign bodies from the eye.

*Contraindications:* This preparation is contraindicated in persons with a history of hypersensitivity to any of its ingredients.

*Adverse Reactions and Precautions:* The preparation is not intended for the treatment of deep-seated infections of the eye. Although hypersensitivity reactions to the components are unlikely, medication should be discontinued if signs of irritation appear.

As with any antibiotic preparation, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Constant observation of the patient is essential. Should superinfection occur, the preparation should be discontinued and/or appropriate therapy instituted.

*Administration and Dosage:* Half inch or more of ointment column should be applied to the eyelid or conjunctiva as required, usually two to three times a day.

*Supply:* Tubes of 3.6 Gms. with ophthalmic tip.

*Expiration date* 36 months. Keep tightly closed in a cool place.

## SPECTROSULF® DUSTING POWDER — Powder

Squibb Neomycin-Gramicidin (Spectrocin®) with Sulphacetamide

Spectrosulf Dusting Powder is a fine powder designed for topical application on infected surfaces.

Each gramme of Spectrosulf Dusting Powder contains :

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|---|---|
| Sodium Sulphacetamide | 75 mg. |
| Neomycin Sulphate (equivalent to pure base) | 5 mg. |
| Gramicidin | 0.5 mg. |

*Action:* Spectrosulf Dusting Powder is a broad spectrum antibacterial formulation containing three highly effective antibacterial agents, i.e., sodium sulphacetamide, neomycin sulphate and gramicidin. Sodium sulphacetamide is non-irritant when applied locally and is active against a broad range of susceptible organisms. Neomycin sulphate is specially active against gram-negative bacteria, viz. E. coli, A. aerogenes, K. pneumoniae, Proteus vulgaris and H. influenzae, while gramicidin is particularly active against gram-positive bacteria, e.g., streptococci, staphylococci, pneumococci and aerobic sporulating bacilli. None of the ingredients of Spectrosulf Dusting Powder is absorbed when applied locally and hence has no untoward effects. Spectrosulf Dusting Powder has advantages as it acts in the presence of pus and tissue fluids and does not delay wound healing.

*Indications:* Infected ulcers, cuts, wounds, burns, pyoderma and other infected dermatoses.

*Contraindications:* It is contraindicated in patients who are allergic to sulphacetamide and neomycin.

*Adverse Reactions:* Although sensitization reactions to sodium sulphacetamide and neomycin sulphate are rare but have been reported. Otherwise Spectrosulf Dusting Powder is devoid of any significant side effects.

*Administration:* After cleaning the infected surface sprinkle the powder directly by tapping the bottle gently and then apply sterile bandage.

*Supply:* Spectrosulf Dusting Powder is supplied in plastic bottles of 10 Gms.

*Note:* Keep tightly closed in a cool, dry place.

*Expiration date* 24 months.

## STRYCITAL® — Tablets

Squibb Streptomycin with Phthalylsulphacetamide

Strycital is Squibb Streptomycin with Phthalylsulphacetamide supplied as tablets for the control of diarrhoea of bacterial origin.

Each tablet provides:

Streptomycin base (as Sulphate) ..... 0.125 Gm.
Phthalylsulphacetamide ..... 0.250 Gm.

*Action:* Oral administration of a combination of streptomycin and a sulphonamide affords a more rapid and effective sterilization of the intestines than is provided by the administration of either drug alone.

Streptomycin is effective against many of the organisms which commonly infect the intestinal tract. Since streptomycin is poorly absorbed from the gastro-intestinal tract and is not inactivated therein, high concentrations of the orally administered antibiotic are reached in the intestinal contents. Consequently the enteric flora is markedly inhibited and the bacterial content of the faeces is greatly reduced. Oral ingestion of streptomycin is utilized only for local anti-bacterial effects in the intestinal tract. Since oral dosage reduces the intra-intes-tinal bacterial flora, it is of use prophylactically in intestinal surgery and in the treatment of bacillary diarrhoeas.

Phthalylsulphacetamide is absorbed only to a negligible extent after oral adminis-tration, however, high concentrations of phthalylsulphacetamide appear in the lumen of the intestine as well as in the tissues of the intestinal wall, without concomitant production of significant blood levels or appreciable tissue concen-trations anywhere else in the body. High concentrations of phthalylsulphaceta-mide in the bowel wall is especially important to ensure optimal antibacterial action against enteric organisms.

*Advantages:* By virtue of their limited absorption there is practically no danger of unfavourable systemic reactions with orally administered phthalylsulphacetamide and streptomycin.

*Indications:* Strycital Tablets are recommended for the treatment of bacterial enteric infections and diarrhoeal conditions susceptible to phthalylsulphacetamide or streptomycin. Specially, Strycital Tablets are useful in shigellosis, including mild early bacillary dysentery and diarrhoea of non-specific origin, such as infantile diarrhoea and the "summer diarrhoeas". It has also been of benefit in controlling acute attacks of ulcerative colitis.

If the symptoms of dysentery are not controlled within 5 days a review of the case is desirable. In acute fulminating gastroenteritis supportive measures to combat fluid and electrolyte imbalance should be instituted. Strycital Tablets are not recommended for the treatment of typhoid fever and systemic infections.

*Dosage:* Adults: 2-4 tablets administered 3-4 times a day.

Children under 40 Kg. should be given a total dose of 2-6 tablets in divided doses according to the body weight and severity of the disease.

For the pre-operative sterilization of gastrointestinal tract 4 tablets should be administered 4 times a day for 2-3 days before surgery.

*Side Effects:* No unfavourable effects have been reported with Strycital Tablets. Evidence of sulphonamide toxicity or local sensitivity reactions to streptomycin requires discontinuation of treatment.

*Supply:* Boxes of 100 tablets (10 strips of 10's).

*Note:* Strycital Tablets may be stored at room temperature.

*Expiration date* 24 months.

## TALSUTIN® VAGINAL TABLETS — Vaginal Tablets

Squibb Tetracycline and Amphotericin B (Fungizone®)

Tetracycline base (equivalent to 100 mg. tetracycline hydrochloride) and 50 mg. amphotericin B per tablet.

Talsutin Vaginal Tablets are provided as compressed tablets, containing tetracycline base equivalent to 100 mg. tetracycline hydrochloride and 50 mg. amphotericin B for intravaginal administration.

*Action:* Talsutin Vaginal Tablets combine a broad spectrum antibiotic with an antifungal agent and are designed to provide simultaneous antimicrobial, anticandidal and antitrichomonal therapy.

Tetracycline has proved effective therapeutically against a broad spectrum of micro-organisms, including both gram-positive and gram-negative bacteria, spirochaetes, and certain rickettsiae and viruses. While the direct action of tetracycline against *Trichomonas in vitro* is slight, it acts against the bacteria with which *Trichomonas* often exist in symbiosis *in vivo*.

Amphotericin B is a polyene antibiotic with antifungal activity against a wide variety of yeasts and yeast-like fungi, including *Candida* species. Produced by a strain of *Streptomyces nodosus*, Amphotericin B exhibits greater activity *in vitro* than nystatin against *Candida* (Monilia) *albicans*.

*Indications:* Talsutin Vaginal Tablets are indicated in the treatment of candidal, trichomonal and/or bacterial infections of the vagina and cervix. The preparation is also useful in the prevention of secondary infections following cervical cauterization and conization, in the treatment of infectious complications of atrophic or senile vaginitis, in non-specific vaginitis, and in vaginal infections in which an offending organism cannot be identified.

*Contraindications:* The preparation should not be administered to patients with a history of hypersensitivity to any of its components.

*Precautions:* Appropriate measures should be taken to avoid the possibility of reinfection by the sexual partner.

*Adverse Reactions:* Talsutin Vaginal Tablets are virtually nontoxic and nonsensitizing and are usually well tolerated. If irritation occurs, treatment should be discontinued.

*Dosage and Administration:* The usual therapeutic dose is one or two tablets daily, deposited high in the vagina. In most cases two weeks of therapy will be sufficient, but more prolonged treatment may be necessary. It is important that therapy be continued during menstruation. Adjunctive measures such as therapeutic douches are unnecessary and sometimes inadvisable. Cleansing douches may be used by non-pregnant women, if desired, for aesthetic purposes.

If hanging drop preparations or cultures remain positive after one course of therapy, a second or even third course may be given.

The usual prophylactic dose following cervical cauterization or conization is one tablet daily at bedtime, for one week or as required.

*Supply:* Talsutin Vaginal Tablets are supplied in boxes of 24 tablets (6 strips of 4's).

*Note:* Store in a cool, dry place.

*Expiration date* 18 months.

## THERAGRAN®

**Tablets**

Squibb Vitamins for Therapy

Theragran Tablets are indicated in the oral treatment of mixed vitamin deficiencies.

Each Theragran Capsule-shaped Tablet supplies:

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| Vitamin A | 25,000 I.U. |
| Vitamin D | 1,000 I.U. |
| Vitamin $B_1$ (Thiamine Mononitrate) | 10 mg. |
| Vitamin $B_2$ (Riboflavine) | 10 mg. |
| Niacinamide | 100 mg. |
| Vitamin C (as Sodium Ascorbate) | 0.2 Gm. |
| Vitamin $B_6$ (Pyridoxine Hydrochloride) | 5 mg. |
| Calcium Pantothenate | 20 mg. |
| Vitamin $B_{12}$ (as $B_{12}$ activity concentrate oral powder) | 5 mcg. |
| Vitamin E (as d- $\alpha$ - Tocopheryl Acid Succinate) | 15 I.U. |

*Advantages:* Theragran is the most widely recommended high potency vitamin preparation in the world. The formulation is reviewed constantly to assure inclusion of nutritional agents that are known to be important when the patient's physical condition requires nutritional support.

*Indications:* Theragran Tablets supply truly therapeutic dosages of nine vitamins almost invariably associated with chronic vitamin-deficiency states, and of clinical importance whenever nutritional support is required. Clinical research and experience support the use of nutritional therapy in the following acute or chronic situations: infectious disease, arthritis, hepatic disease, the mal-absorption syndrome, degenerative disease, cardiac disease, dermatologic conditions, gastrointestinal conditions (including peptic ulcer), neuroses and psychiatric disorders, diabetes, alcoholism, ulcerative colitis, pancreatitis, osteoporosis, the female climacteric, and pre- and post-operatively.

*Dosage:* One tablet daily, or as indicated.

*Supply:* Bottles of 15 and 100 tablets.

*Note:* Keep tightly closed in a cool place.

*Expiration date* 18 months.

## THERAGRAN® PEDIATRIC DROPS — Liquid

Squibb Multiple Vitamin Drops

Theragran Pediatric Drops, Squibb Multiple Vitamin Drops, is a pleasant-tasting fruit flavoured solution preserved with 0.1% sodium benzoate and 0.02% methyl parahydroxybenzoate, containing balanced amount of the essential vitamins in a convenient drop-dosage form. Because of its palatability, Theragran Pediatric Drops are well accepted by infants and children.

Each 0.6 ml. supplies:

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|---|---|
| Vitamin A | 5,000 I.U. |
| Vitamin $D_3$ | 1,000 I.U. |
| Vitamin $B_1$ (Thiamine Hydrochloride) | 1.2 mg. |
| Vitamin $B_2$ (as Riboflavine-5-Phosphate Sodium) | 2.0 mg. |
| Vitamin $B_6$ (Pyridoxine Hydrochloride) | 2.0 mg. |
| Vitamin C | 70.0 mg. |
| Niacinamide | 12.0 mg. |
| d-Panthenol | 5.0 mg. |

*Indications:* Deficiencies of a single vitamin are practically impossible in infants and children, since most nutritional deficiency states involve multiple factors. If a patient is deficient in one vitamin, he is invariably deficient in other essential vitamins. Because of its high content of various vitamin components, Theragran Pediatric Drops are particularly useful in infants and children in preventing and treating rickets, scurvy, beriberi, pellagra and a wide variety of other syndromes caused by metabolic disturbances in connection with the various avitaminoses. It is also recommended for prophylactic use in patients with an inadequate vitamin intake, in cases where vitamin requirements have increased or in patients whose condition is such that vitamin absorption and utilization are impaired.

Theragran Pediatric Drops are especially valuable during convalescence and during periods of active development of tissue repair.

*Advantages:* Theragran Pediatric Drops are convenient to give and easy to take. It mixes easily with milk, soups, cereals, puddings and juices, or it may be placed directly on the tongue. Also, it will not change the taste of food appreciably (if at all), and can often be given without the patient's knowledge, thus surmounting the psychological barrier to medication so often encountered in paediatrics. This dosage form is particularly suited for infants, children and patients who have difficulty in taking tablets and/or capsules.

*Dosage: Prophylactic Dose:* 0.3 ml. daily for infants and children up to 4 years
0.6 ml. daily for older children

*Therapeutic Dose:* As directed by the physician.

*Supply:* Bottles of 10 ml. with dropper scored at 0.3 ml. and 0.6 ml.

*Note:* Keep in a cool place.

*Expiration date* 12 months.

## THERAGRAN-GR®

**Tablets**

Squibb Anabolic Sex Hormones with Vitamins and Minerals

Theragran-GR (anabolic sex hormones with vitamins and minerals) is an oral preparation providing full therapeutic amounts of anabolic steroid hormones in an optimally balanced combination. It also contains fully protective amounts of vitamins for comprehensive nutritional support, with added minerals.

Each Theragran-GR Tablet contains:

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|---|---|
| ANABOLIC SEX HORMONES | |
| Ethinyl Oestradiol | 8 mcg. |
| Methyltestosterone | 4 mg. |
| VITAMINS | |
| A (as Acetate) | 2500 U.S.P. units |
| $B_1$ (Thiamine Mononitrate) | 2.5 mg. |
| $B_2$ (Riboflavine) | 1.5 mg. |
| $B_6$ (Pyridoxine Hydrochloride) | 1 mg. |
| $B_{12}$ (as Cyanocobalamin) | 1 mcg. |
| C (as Sodium Ascorbate) | 37.5 mg. |
| Calcium Pantothenate | 2.5 mg. |
| D (Ergocalciferol) | 250 U.S.P. units |
| E (as d-α-Tocopheryl Acid Succinate) | 2.5 I.U. |
| Folic Acid | 0.1 mg. |
| Niacinamide | 10 mg. |
| MINERALS | |
| Copper (as Sulphate) | 0.5 mg. |
| Iodine (as Potassium Iodide) | 0.05 mg. |
| Iron, elemental (as dried Ferrous Sulphate) | 5 mg. |
| Magnesium (as Oxide) | 3 mg. |
| Manganese (as Sulphate) | 0.5 mg. |
| Zinc (as Sulphate) | 0.5 mg. |

*Action:* The androgen-oestrogen ratio in Theragran-GR Tablets has been designed to provide the closest approximation of endogenous hormone production. Theragran-GR provides greater stimulation of anabolic and hormone homeostatic processes with less likelihood of undesired effects than does therapy with either androgen or oestrogen alone.

Androgen and oestrogen have opposing effects on the genital and accessory sexual structures of men and women. The balanced androgen-oestrogen ratio of Theragran-GR reduces to a minimum the occurrence of unwanted effects such as masculinization of the female and feminization of the male.

The complementary stimulatory actions of the two steroids in Theragran-GR offer an increased potential for the anabolism of protein and osseous tissues, and for the maintenance of the psychic and nervous system equilibrium at the physiological level of the well-adjusted, mature man or woman.

The separate inhibitory actions of the two steroids on gonadotropic hormone production and release assure an increased potential for the correction of hormonal imbalance such as exists during the climacteric state. Theragran-GR helps check the hot flushes, sweating, insomnia, headache and peripheral circulatory disturbances associated with the female climacteric. In the male climacteric Theragran-GR helps the patient maintain psychic equilibrium.

Vitamins with added minerals have been included in the formula to help the body meet the increased demand for these essentials during anabolism. Because Theragran-GR contains fully protective amounts of vitamins, elderly patients in particular will benefit from this comprehensive nutritional support, and since the diets of such patients are frequently inadequate, they commonly have a greater need for vitamin-mineral supplementation than any other age group.

*Indications:* Theragran-GR is indicated—

1. During and following the menopause for prompt relief from the clinical symptoms of the menopause, such as emotional instability, hot flushes, sweating, insomnia, headaches, and peripheral vascular disturbances. The sequelae of the menopause, while often less striking than the early symptoms, may be far more distressing and damaging. The lowered supply of anabolic steroids following the menopause may be inadequate to provide for the metabolic needs of protein and osseous tissues.
2. During and following the male climacteric.
3. Tissue atrophy and/or mild psychic disturbances in geriatric patients.
4. Protein depletion and chronic debility following malnutrition, infection, trauma, surgery or prolonged illness in geriatric patients.
5. Osteoporosis (postmenopausal, senile, and other types).

*Contraindications:* Theragran-GR is not recommended for patients with a history of established or suspected mammary or genital (including prostatic) malignancy.

*Precautions:* While folic acid may correct the blood picture of pernicious anaemia, it may not ameliorate the attendant neurologic involvement. The possibility of this condition should be excluded before treatment.

*Adverse Reactions:* When administered in therapeutic dosage, Theragran-GR generally produces a minimum of undesired effects. However, because the normal endogenous hormonal production and tissue responsiveness vary individually, certain patients may be overly reactive to either androgenic or oestrogenic medication.

Unwanted effects (virilization, uterine bleeding, mastodynia) may be controlled by temporarily reducing dosage or by discontinuing medication entirely.

Patients receiving steroid medication should also be observed for oedema. This may be combated by temporarily reducing or omitting the medication, by instituting a low-salt diet or by the use of a suitable diuretic.

*Dosage:* The average adult dosage is 2 tablets daily. Dosage should be increased or lowered in accordance with individual response.

When Theragran-GR is used to continue the benefits of long-acting parenteral androgen-oestrogen therapy, the oral medication should be started three weeks after the time of the last injection, or before this if symptoms have reappeared. When parenteral androgen-oestrogen therapy is given to replace Theragran-GR, the oral medication may be continued for two or three more days following the initial injection.

*Supply:* Boxes of 100 tablets (10 strips of 10's).

*Note:* Keep in a cool place.

*Expiration date* 18 months.

## THERAGRAN®-M

**Tablets**

Squibb Vitamins-Minerals for Therapy

A high potency vitamin formula with added minerals and trace elements.

Each capsule-shaped tablet contains:

VITAMINS

| | |
|---|---|
| Vitamin A | 25,000 I.U. |
| Vitamin D | 1,000 I.U. |
| Vitamin C | 200 mg. |
| Thiamine Mononitrate ($B_1$) | 10 mg. |
| Riboflavine ($B_2$) | 10 mg. |
| Niacinamide | 100 mg. |
| Pyridoxine Hydrochloride ($B_6$) | 5 mg. |
| Calcium Pantothenate | 20 mg. |
| Vitamin E | 15 I.U. |
| Cyanocobalamin ($B_{12}$) | 5 mcg. |

MINERALS

| | |
|---|---|
| Potassium Iodide (equivalent to 0.15 mg. Iodine) | 0.2 mg. |
| Dried Ferrous Sulphate (equivalent to 12 mg. Iron) | 41 mg. |
| Copper Sulphate (equivalent to 2 mg. Copper) | 8 mg. |
| Manganese Sulphate (equivalent to 1 mg. Manganese) | 2.8 mg. |
| Magnesium Carbonate (equivalent to 65 mg. Magnesium) | 270 mg. |
| Zinc Sulphate (equivalent to 1.5 mg. Zinc) | 6.6 mg. |

*Action and Uses:* Theragran-M is indicated in mixed vitamin and mineral deficiencies. Theragran-M supplies high potency dosages of vitamins and minerals associated with chronic vitamin deficiency states, and is of clinical importance when high potency nutritional support is indicated in special medical situations such as infectious disease, arthritis, hepatic disease, the malabsorption syndrome, degenerative disease, cardiac disease, dermatologic conditions, gastrointestinal conditions (including peptic ulcer, ulcerative colitis), psychiatric disorders, diabetes, alcoholism, pancreatitis, osteoporosis, menopause, and pre- and post-operatively.

*Administration and Dosage:* Adults and older children, 1 tablet daily or as recommended.

*Supply:* Boxes of 100 tablets (10 strips of 10's).

*Note:* Keep in a cool place.

*Expiraton date* 18 months.

## THERAGRAN® SYRUP

**Syrup**

Squibb Multivitamin Tonic with Lysine and Iron

Theragran Syrup is a pleasantly flavoured multivitamin tonic fortified with especially formulated lysine and iron for children. It can also be recommended for patients who prefer a liquid preparation.

Each 5 ml. provides:

| | |
|---|---|
| Vitamin A (as Palmitate) | 3000 I.U. |
| Vitamin $D_3$ | 500 I.U. |
| Thiamine HCl ($B_1$) | 1.5 mg. |
| Vitamin $B_2$ (as Riboflavine-5-Phosphate Sodium) | 1.5 mg. |
| Niacinamide | 10 mg. |
| Pyridoxine HCl ($B_6$) | 1 mg. |
| d-Panthenol | 2.5 mg. |
| Cyanocobalamin ($B_{12}$) | 5.0 mcg. |
| Vitamin C | 50 mg. |
| Lysine Monohydrochloride | 100 mg. |
| Ferrous Gluconate | 26 mg. |

In a pleasantly flavoured syrup base. (Extra vitamins added to compensate for loss on storage.)

*Action and Uses:* Theragran Syrup is designed to supply essential vitamins. It provides nutritional support and is indicated in mixed vitamin deficiencies.

It is of particular value in special medical conditions such as infectious disease, hepatic disease, malabsorption syndromes, improper food intake or utilisation and in physiological conditions where increased amounts of essential vitamins are required. Theragran Syrup is also useful as a general daily dietary supplement for prophylaxis of vitamin deficiencies. Besides extra essential vitamins, children need adequate amount of lysine and iron for their proper growth. Theragran Syrup provides both and hence is an ideal tonic for the optimum growth and development of adolescent.

*Dosage:* For children between 2-12 years, one teaspoonful (5 ml.) once or twice a day is recommended. As a dietary supplementation, one teaspoonful daily is adequate.

*Supply:* Bottles of 60 ml.

*Note:* Keep tightly closed in a cool place. Protected from light.

*Expiration date* 12 months.

## TOSSEX® EXPECTORANT

**Syrup**

Squibb Carbetopentane Citrate with Expectorant

Tossex Expectorant is a cough syrup which combines the superior cough depressant effect of carbetopentane citrate [2-(2 diethyl-aminoethoxyl) ethanol 1-phenylcyclopentyl carboxylate citrate] with the well recognised expectorant effect of terpin hydrate and the demulcent action of sodium citrate.

Each 5 ml. (approximately one teaspoonful) of Tossex Expectorant contains:

| | |
|---|---|
| Carbetopentane Citrate | 10.65 mg. |
| Terpin Hydrate | 15.00 mg. |
| Sodium Citrate | 65.00 mg. |
| Alcohol | 0.25 ml. |

in a pleasant-tasting, fruit-flavoured, glycerine-syrup base.

*Action:* Carbetopentane citrate is a synthetic cough depressant and is non-narcotic. The main property of carbetopentane citrate is its temporary effect on cough reflex, most probably through its effect on the cough centre. It has an antitussive activity which equals 150% of that of codeine, as shown in animal experiments. Terpin hydrate exerts an expectorant action to lessen an abundant sputum especially in chronic coughs. Sodium citrate loosens and reduces the viscosity of the mucus secretion helping its prompt removal.

*Indications:* Tossex Expectorant is indicated in all types of cough. It is specially useful for the relief of all dry, irritating and unproductive coughs. Tossex Expectorant is the ideal therapy for the management of a wide variety of clinical conditions such as:

— cough associated with affections of the respiratory tract: rhinopharyngitis, laryngitis, tracheobronchitis, bronchopneumonia, influenza, common cold
— cough following emphysematous lesions or pleural irritations
— intractable coughs of bacillosis, pulmonary neoplasm, bronchiectasis
— the irritating cough of tuberculosis
— smokers' cough
— spasmodic cough

*Advantages:*

* combines a superior cough depressant with well recognized expectorants
* has a pleasant taste—even children take it without complaint
* controls even severe coughs associated with a variety of disorders
* does not contain any narcotic; therefore, it does not possess the danger of addiction seen with morphine and its derivatives
* does not cause any of the central effects of opiates
* does not cause constipation, and is well tolerated in gastrointestinal tract
* no general toxic effects have yet been observed

*Dosage: For adults and children over 12 years:* 2 to 4 teaspoonfuls three or four times a day.
*For children 2 to 12 years:* 1 teaspoonful three or four times a day.
*For infants below 2 years:* ½ teaspoonful three or four times a day.

*Side Effects:* Tossex Expectorant is usually well tolerated and causes neither constipation nor apparent action upon the nervous system. Only rarely digestive complaints and skin rashes may be observed. Such medication has been used for period ranging from four weeks to four months without any evidence of intolerance or harmful side effects.

*Supply:* Bottles of 70 ml. and 120 ml.

## VIGRAN® with $B_{12}$ — Capsules

Squibb Vitamins for Maintenance

A multivitamin preparation for routine use as a dietary supplement in the prevention of vitamin deficiencies.

Each Vigran Capsule supplies the following vitamins:

| | |
|---|---|
| Vitamin A | 5,000 I.U. |
| Vitamin D | 500 I.U. |
| Thiamine Mononitrate | 2 mg. |
| Riboflavine | 2 mg. |
| Pyridoxine Hydrochloride | 0.5 mg. |
| Pantothenic Acid (as Calcium Pantothenate) | 1 mg. |
| Niacinamide | 20 mg. |
| Ascorbic Acid | 45 mg. |
| Vitamin $B_{12}$ | 2 mcg. |

*Indications:* Vigran is used as a supplement to the diet; for the prevention of deficiencies of these vitamins.

*Dosage:* One capsule daily.

*Supply:* Bottles of 25 and 100 capsules.

*Note:* Keep in a cool place.

*Expiration date* 24 months.

## VIMGRAN®

**Tablets**

Squibb Vitamins-Minerals for Maintenance

Vimgran is a vitamin and mineral formula for maintenance. Each Vimgran tablet provides 100% or more of the minimum daily requirements, vitamins A, $B_1$, $B_2$, C, D, and niacinamide for adults and children, as well as other vitamins, plus minerals and trace elements, caloric equivalent is 2 calories per tablet.

Each Vimgran Tablet contains:

VITAMINS

| | |
|---|---|
| Vitamin A (as Acetate) | 5,000 I.U. |
| Vitamin D (Irrad. Ergosterol) | 500 I.U. |
| Vitamin $B_1$ (Thiamine Mononitrate) | 3.0 mg. |
| Vitamin $B_2$ (Riboflavine) | 3.0 mg. |
| Vitamin $B_6$ (Pyridoxine Hydrochloride) | 1.0 mg. |
| Vitamin $B_{12}$ (Cyanocobalamin) | 2.0 mcg. |
| Calcium Pantothenate | 5.0 mg. |
| Niacinamide | 20.0 mg. |
| Vitamin C (as Sodium Ascorbate) | 50.0 mg. |
| Vitamin E (as d-$\alpha$-Tocopheryl Acid Succinate) | 5.1 I.U. |
| Folic Acid | 0.1 mg. |

MINERALS

| | |
|---|---|
| Calcium Carbonate (equi. to 100 mg. Calcium) | 250 mg. |
| Ferrous Sulphate exsiccated (equi. to 10 mg. Iron) | 34 mg. |
| Potassium Iodide (equi. to 0.15 mg. Iodine) | 0.2 mg. |
| Potassium Sulphate (equi. to 5 mg. Potassium) | 11.0 mg. |
| Copper Sulphate (equi. to 1 mg. Copper) | 4.0 mg. |
| Manganese Sulphate (equi. to 1 mg. Manganese) | 2.8 mg. |
| Zinc Sulphate (equi. to 1.5 mg. Zinc) | 6.6 mg. |
| Magnesium Oxide (equi. to 6 mg. Magnesium) | 10.0 mg. |

*Advantages:* Vanillin coated tablet minimizes "vitamin taste". Vitamin "aftertaste" occurs rarely.

*Indications:* To help prevent vitamin and mineral deficiencies.

*Dosage:* One tablet daily or as recommended.

*Supply:* Boxes of 100 tablets (10 strips of 10's).

*Expiration date* 18 months.

## YEAST, BREWERS', SQUIBB — Tablets

Squibb Brewers' Yeast Tablets are an exceptionally rich source of all the naturally occurring B Complex vitamins. These tablets are not artificially fortified.

Each 0.35 Gm. Squibb Brewers' Yeast Tablet supplies:

| | |
|---|---|
| Thiamine ($B_1$) | 0.035 mg. |
| Riboflavine ($B_2$) | 0.015 mg. |
| Niacin | 0.125 mg. |

In addition, each tablet contains the other factors of the B Complex commonly occurring in yeast.

*Indications:* Squibb Brewers' Yeast Tablets are a useful adjunct to the diets of persons who are not eating the right kind of food every day. For persons such as these, Squibb Brewers' Yeast Tablets can supply significant amounts of the whole, natural B Complex.

*Advantages:* The yeast in Squibb Brewers' Yeast Tablets is especially grown for medicinal use. It is not a debittered yeast obtained as a by-product of the brewing industry.

Squibb Brewers' Yeast Tablets are exceptionally palatable because they are flavoured to enhance the nutty taste of the yeast.

*Dosage:* To fortify a deficient diet, 12 Squibb Brewers' Yeast Tablets should be taken daily. When the food intake is very limited by serious illness, more tablets may be used.

*Supply:* Bottles of 100 and 1,000 tablets.

*Note:* Keep in a cool place.

*Expiration date* 24 months.

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# PHARMACOLOGIC INDEX

# NORMAL LABORATORY VALUES OF CLINICAL IMPORTANCE*

## NORMAL BLOOD, PLASMA AND SERUM VALUES

For some procedures the normal values may vary, depending upon the methods used.

### CHEMICAL CONSTITUENTS

| | |
|---|---|
| Acetone, serum | 0.3-2.0 mg./100 ml. |
| Aldolase, serum Male | Less than 33 units |
| Female | Less than 19 units |
| Alpha amino nitrogen, plasma | 3.0-5.5 mg./100 ml. |
| Ammonia, blood | 40-70 microgm./100 ml. |
| Amylase, serum | 80-180 Somogyi units/100 ml. |
| Ascorbic acid, blood | 0.4-1.5 mg./100 ml. |
| Barbiturates, serum | 0 |
| | Coma level: Phenobarbital approximately 11 mg./100 ml.; most other barbiturates 1.5 mg./100 ml. |
| Base, total, serum | 145-160 mEq./l. |
| Bilirubin, serum | |
| Direct | 0.1-0.4 mg./100 ml. |
| Indirect | 0.2-0.7 mg./100 ml. |
| | (Total minus direct) |
| Total | 0.3-1.1 mg./100 ml. |
| Bromides, serum | 0 |
| | Toxic levels above 17 mEq./l. |
| Calcium, serum | 4.5-5.5 mEq./l. |
| | (9.0-11.0 mg./100 ml.) |
| | (Slightly higher in children) |
| | (Varies with protein concentration) |
| Ionized | 2.1-2.6 mEq./l. |
| | (4.25-5.25 mg./100 ml.) |
| Carbon dioxide, serum | |
| Content | 26-28 mEq./l. |
| | Infants: 20-26 mEq./l. |
| Combining power | 24-29 mEq./l. |
| | (53-64 vol. per cent) |
| Tension, $pCO_2$ | 35-45 mm. Hg. |
| Carbon monoxide, blood | Symptoms with over 20% saturation |
| Carotenoids, serum | 100-300 I.U./100 ml. |
| Chloride, serum | 100-106 mEq./l. |
| | (355-376 mg./100 ml. as Cl) |
| | (585-620 mg./100 ml. as NaCl) |
| Cholesterol, serum | |
| Total | 150-250 mg./100 ml. |
| Esters | 68-76% of total cholesterol |
| Copper, serum | 70-140 microgm./100 ml. |
| Creatine, serum | 0.2-0.8 mg./100 ml. |

* Taken from "A Textbook of Medicine" edited by Russel L. Cecil and Robert F. Loeb, W. B. Saunders Company, 12th edition.

**Normal Blood, Plasma and Serum Values** – *Contd.*

| | | |
|---|---|---|
| Creatinine, serum | | 0.7-1.5 mg./100 ml. |
| Cryoglobulins, serum | | 0 |
| Dilantin, blood or serum | | Therapeutic levels 1-11 microgm./ml. |
| Ethanol, blood | | |
| Marked intoxication | | 0.3-0.4% |
| Alcoholic stupor | | 0.4-0.5% |
| Coma | | Above 0.5% |
| Fibrinogen, plasma | | 200-400 mg./100 ml. |
| Glucose (fasting), blood | | |
| True | | 60-100 mg./100 ml. |
| Folin | | 80-120 mg./100 ml. |
| 17-Hydroxycorticoids, plasma | | 5-25 microgm./100 ml. |
| Icterus index, serum | | 4-7 |
| Iodine, butanol extractable, serum | | 3.5-6.5 microgm./100 ml. |
| Iodine, protein bound, serum | | 3.5-8.0 microgm./100 ml. (Maybeslightlyhigherininfants) |
| Iron, serum | | 75-175 microgm./100 ml. |
| Iron binding capacity, unsaturated, serum | | 150-300 microgm./100 ml. |
| Lactic acid, blood | | 6-16 mg./100 ml. |
| Lactic dehydrogenase, serum | | 200-450 units/ml. |
| Lead, blood | | 0-50 microgm./100 ml. |
| Lipase, serum | | Less than 1.5 units (ml. of N/20 NaOH) |
| Lipids, total, serum | | 450-850 mg./100 ml. |
| Lipid partition, serum | | |
| Cholesterol | | 150-250 mg./100 ml. |
| Cholesterol esters | | 68-76% of total cholesterol |
| Phospholipids | | 6-12 mg./100 ml. as lipid phosphorus |
| Total fatty acids | | 190-420 mg./100 ml. |
| Neutral fat | | 0-150 mg./100 ml. |
| Magnesium, serum | | 1.5-2.5 mEq./l. (1.8-3.0 mg./100 ml.) |
| Nitrogen, nonprotein, serum | | 15-35 mg./100 ml. |
| Osmolality, serum | | 285-295 mOsm./l. |
| Oxygen, blood | | |
| Capacity | | 16-24 vol. % (varies with Hb.) |
| Content | Arterial | 15-23 vol. per cent |
| | Venous | 10-16 vol. per cent |
| Saturation | Arterial | 94-100% of capacity |
| | Venous | 60-85% of capacity |
| Tension, $pO_2$ | Arterial | 95-100 mm. Hg. |
| pH, arterial, plasma | | 7.35-7.45 |
| Phenylalanine, serum | | Less than 3 mg./100 ml. |
| Phosphatase, acid, serum | | 1.0-5.0 units (King-Armstrong)<br>0.5-2.0 units (Bodansky)<br>0.5-2.0 units (Gutman)<br>0.0-1.1 units (Shinowara)<br>0.1-0.63 units (Bessey-Lowry) |

**Normal Blood, Plasma and Serum Values** – *Contd.*

| | |
|---|---|
| Phosphatase, alkaline, serum | 5.0-13.0 units (King - Armstrong)<br>2.0-4.5 units (Bodansky)<br>3.0-10.0 units (Gutman)<br>2.2-8.6 units (Shinowara)<br>0.8-2.3 units (Bessey-Lowry)<br>(Values are higher in children.) |
| Phosphate, inorganic, serum | 3.0-4.5 mg./100 ml.<br>(children, 4.0-7.0 mg./100 ml.) |
| Potassium, serum | 3.5-5.0 mEq./l.<br>(14-20 mg./100 ml. as K) |
| Proteins, serum | |
| Total | 6.0-8.0 gm./100 ml. |
| Albumin | 3.5-5.5 gm./100 ml. |
| Globulin | 1.5-3.0 gm./100 ml. |
| Paper electrophoresis | |
| Albumin | 45-55% of total |
| Globulin | |
| $Alpha_1$ | 5-8% of total |
| $Alpha_2$ | 8-13% of total |
| Beta | 11-17% of total |
| Gamma | 15-25% of total |
| Pyruvic acid, plasma | 1.0-2.0 mg./100 ml. |
| Salicylate, plasma | 0 |
| Therapeutic range | 20-25 mg./100 ml. |
| Toxic range | Over 30 mg./100 ml. |
| Serotonin | |
| Platelet suspension | 0.1-0.3 microgm./ml. blood |
| Serum | 0.10-0.32 microgm./ml. |
| Sodium, serum | 136-145 mEq./l.<br>(313-334 mg./100 ml. as Na) |
| Transaminase, serum | |
| S.G.O.T. | 5-40 units/ml. |
| S.G.P.T. | 5-35 units/ml. |
| Urea nitrogen, blood (B.U.N.) | 10-20 mg./100 ml. |
| Uric acid, serum | 3.0-6.0 mg./100 ml. |
| Vitamin A, serum | 30-100 units/100 ml. |

## HEMATOLOGIC EXAMINATIONS

*Bone Marrow* (Relative Number of Nucleated Cells in Normal Bone Marrow)

| | *Range* | *Average* |
|---|---|---|
| Myeloblasts | 0.3 - 5.0 | 2.0 |
| Promyelocytes | 1.0 - 8.0 | 5.0 |
| Myelocytes: neutrophilic | 5.0 -19.0 | 12.0 |
| eosinophilic | 0.5 -19.0 | 1.5 |
| basophilic | 0.0 - 0.5 | 0.3 |
| Metamyelocytes ("juvenile" forms) | 13.0 -32.0 | 22.0 |
| Polymorphonuclear neutrophils | 7.0 -30.0 | 20.0 |
| Polymorphonuclear eosinophils | 0.5 - 4.0 | 2.0 |
| Polymorphonuclear basophils | 0.0 - 0.7 | 0.2 |

| | | |
|---|---|---|
| Lymphocytes | 3.0-17.0 | 10.0 |
| Plasma cells | 0.0- 2.0 | 0.4 |
| Monocytes | 0.5- 5.0 | 2.0 |
| Reticulum cells | 0.2- 2.0 | 0.2 |
| Megakaryocytes | 0.03-3.0 | 0.4 |
| Pronormoblasts | 1.0- 8.0 | 4.0 |
| Normoblasts | 7.0-32.0 | 18.0 |

*Erythrocytes* (See table below)

Fragility, Osmotic
- Slight hemolysis ..... 0.45-0.39%
- Complete hemolysis ..... 0.33-0.30%

Hemochromogens in plasma ..... 3-5 mg./100 ml.

"Life Span"
- Normal survival ..... 120 days
- Chromium, half-life (T ½) ..... 28 days

Plasma iron turnover rate ..... 38 mg./24 hr. (0.47 mg./kg.)

Protoporphyrin, free erythrocyte (E.P.) ..... 20-38 mcg./100 ml. RBCs.

Reticulocytes ..... 0.5-2.0% of red cells

Sedimentation rate

Westergren ..... <15 mm./1 hr.

Wintrobe, Male ..... 0-9 mm./1 hr.

Female ..... 0-20 mm./1 hr.

NORMAL VALUES AT VARIOUS AGES

| Age | Red cell count, millions/cu. mm. | Hemoglobin, Gm./100 ml. | Vol. packed RBC, ml./100 ml. | Corpuscular values | | | |
|---|---|---|---|---|---|---|---|
| | | | | MCV, cuμ | MCH, γγ | MCHC, % | MCD, μ |
| First day | 5.1±1.0* | 19.5±5.0* | 54.0±10.0* | 106 | 38 | 36 | 8.6 |
| 2-3 days | 5.1 | 19.0 | 53.5 | 105 | 37 | 35 | |
| 4-8 days | 5.1 | 18.3±4.0 | 52.5 | 103 | 36 | 35 | |
| 9-13 days | 5.0 | 16.5 | 49.0 | 98 | 33 | 34 | |
| 14-60 days | 4.7±0.9 | 14.0±3.3 | 42.0±7.0 | 90 | 30 | 33 | 8.1 |
| 3-5 mo. | 4.5±0.7 | 12.2±2.3 | 36.0 | 80 | 27 | 34 | 7.7 |
| 6-11 mo. | 4.6 | 11.8 | 35.5±5.0 | 77 | 26 | 33 | 7.4 |
| 1 yr. | 4.5 | 11.2 | 35.0 | 78 | 25 | 32 | 7.3 |
| 2 yr. | 4.6 | 11.5 | 35.5 | 77 | 25 | 32 | |
| 3 yr. | 4.5 | 12.5 | 36.0 | 80 | 27 | 35 | 7.4 |
| 4 yr. | 4.6±0.6 | 12.6 | 37.0 | 80 | 27 | 34 | |
| 5 yr. | 4.6 | 12.6 | 37.0 | 80 | 27 | 34 | |
| 6-10 yr. | 4.7 | 12.9 | 37.5 | 80 | 27 | 34 | 7.4 |
| 11-15 yr. | 4.8 | 13.4 | 39.0 | 82 | 28 | 34 | |
| Adults: | | | | | | | |
| Females | 4.8±0.6 | 14.0±2.0 | 42.0±5.0 | 87±5 | 29±2 | 34±2 | 7.5±0.3 |
| Males | 5.4±0.8 | 16.0±2.0 | 47.0±7.0 | 87±5 | 29±2 | 34±2 | 7.5±0.3 |

MCV = mean corpuscular volume. MCH = mean corpuscular hemoglobin. MCHC = mean corpuscular hemoglobin concentration. MCD = mean corpuscular diameter. (*Wintrobe: "Clinical Hematology", 5th ed., Philadelphia, Lea & Febiger,* 1961.)

* The range of values represents almost the extremes of observed variations (93 per cent or more) at sea level. The blood values of healthy persons should fall well within these figures.

*Leukocytes*

NORMAL VALUES

| | Per cent | Average | Minimum | Maximum |
|---|---|---|---|---|
| Total number, per cu mm | | 7,000 | 5,000 | 10,000 |
| Neutrophils: | | | | |
| Juvenile | 3-5 | 300 | 150 | 400 |
| Segmented | 54-62 | 4,000 | 3,000 | 5,800 |
| Eosinophils | 1-3 | 200 | 50 | 250 |
| Basophils | 0-0.75 | 25 | 15 | 50 |
| Lymphocytes | 25-33 | 2,100 | 1,500 | 3,000 |
| Monocytes | 3-7 | 375 | 285 | 500 |

*Platelets and Coagulation*

Platelets, per cu. mm., direct counting method .. 200,000-300,000
Bleeding time (Ivy method), majority and range.. 1-5 mm., 0-12 min.
Clot retraction time..... Begins in 30 min., complete in less than 24 hr., usually < 6 hr.
Coagulation time (Lee-White method), majority and range..... 5-15 min., 2-19 min.

*Schilling Test*

Excretion in urine of orally administered radioactive vitamin $B_{12}$ following "flushing" parenteral injection of $B_{12}$..... 7-22%

## NORMAL VALUES FOR URINE

Acetone and acetoacetate..... 0
Addis count
Erythrocytes ..... 0-130,000/24 hrs.
Leukocytes..... 0-650,000/24 hrs.
Casts (hyaline)..... 0-2,000/24 hrs.
Aldosterone..... 6-16 microgm./24 hrs.
Alpha amino nitrogen..... 64-199 mg./24 hrs. (not over 1.5% of total nitrogen)
Ammonia..... 20-70 mEq./l.
Amylase (Somogyi) ..... 260-950 Somogyi units/24 hrs.
Calcium
Low Ca diet (Bauer-Aub)..... Less than 150 mg./24 hrs.
Usual diet ..... Less than 250 mg./24 hrs.
Catecholamines
Epinephrine..... Less than 10 microgm./24 hrs.
Norepinephrine ..... Less than 100 microgm./24 hrs.
Chorionic gonadotropin ..... 0
Coproporphyrin..... 50-250 microgm./24 hrs.
Creatine..... Less than 100 mg./24 hrs. (Higher in children and during pregnancy)

| | |
|---|---|
| Creatinine | 15-25mg./kg. of body wt./24 hrs. |
| Cystine or cysteine | 0 |
| Estrogens | |
| Male | 4-25 microgm./24 hrs. |
| Female | 4-60 microgm./24 hrs. (Increased during pregnancy) |
| Hemoglobin and myoglobin | 0 |
| Homogentisic acid | 0 |
| 5-Hydroxyindole-acetic acid (5-HIAA) | |
| Qualitative | 0 |
| Quantitative | Less than 16 mg./24 hrs. |
| 17-hydroxycorticoids Male | 5-15 mg./24 hrs. |
| Female | 4-10 mg./24 hrs. (Varies with method used) |
| 17-ketosteroids | |
| Under 8 years | 0-2 mg./24 hrs. |
| Adolescents | 2-20 mg./24 hrs. |
| Male | 8-25 mg./24 hrs. |
| Female | 5-15 mg./24 hrs. |
| Lead | Less than 0.08 microgm./ml. or Less than 120 microgm./24 hrs. |
| pH | 4.6-8.0 average 6.0 (Depends on diet) |
| Phenylpyruvic acid | 0 |
| Pituitary gonadotropins | 5-10 rat units/24 hrs. 10-50 mouse units/24 hrs. (Increased after menopause) |
| Porphobilinogen | 0 |
| Protein | 0 qualitative (Less than 30 mg./24 hrs.) |
| Specific gravity | 1.003-1.030 |
| Solids, total | 30-70 gm./l., average 50 gm./l. (To estimate total solids per liter, multiply last two figures of specific gravity by 2.66, Long's coefficient.) |
| Sugar | 0 |
| Titrable acidity | 20-40 mEq./24 hrs. |
| Urobilinogen | Up to 1.0 Ehrlich units/2 (1-3 P.M.) 0-4.0 mg./24 hrs. |
| Vanillylmandelic acid (VMA) | 1.8-8.4 mg./24 hrs. |

## NORMAL VALUES FOR STOOL

| | |
|---|---|
| Bulk | 100-200 gm. daily |
| Water content | Approximately 65% |
| Dry matter | 23-32 gm. daily |
| Protein content | Minimal |
| Fat, total | 17.5% of dry matter (Up to 30% of dry weight is normal) |

| | |
|---|---|
| Fatty acid combined as soap | 4.6% of dry matter |
| Free fatty acid | 5.6% of dry matter |
| Neutral fat | 7.3% of dry matter |
| | (42% of total fat) |
| Nitrogen excretion | Less than 1.7 gm./day |
| Urobilinogen | 40-280 mg./24 hours |

## NORMAL VALUES FOR CEREBROSPINAL FLUID

| | |
|---|---|
| Cells | Fewer than 5 per cu. mm.,all mononuclear |
| Chloride | 120-130 mEq./l. |
| | (20 mEq./l. higher than serum) |
| Colloidal gold test | Not more than 1 in any tube |
| Gamma globulin | 1.3-4.7 mg./100 ml. |
| | 4.3-12.3% of total protein |
| Glucose | 50-75 mg./100 ml. |
| | (20 mg./100 ml. less than blood) |
| Pressure | 70-180 mm. water |
| Protein | 15-45 mg./100 ml. |

## NORMAL VALUES FOR GASTRIC ANALYSIS

| | | |
|---|---|---|
| Acidity | | |
| Fasting | Free acidity | 0-30 degrees/100 ml. |
| | Total acidity | 10-50 degrees/100 ml. |
| One hour after histamine | | |
| | Free acid | 30-85 degrees/100 ml. |
| Diagnex blue (Squibb) | Anacidity | 0-0.3 mg. in 2 hours |
| | Doubtful | 0.3-0.6 mg. in 2 hours |
| | Normal | Greater than 0.6 mg. in 2 hours |
| Volume, fasting stomach content | | 50-100 ml. |
| Emptying time | | 3-6 hours |
| Color | | Opalescent or colorless |
| Specific gravity | | 1.006-1.009 |
| pH (adults) | | 0.9-1.5 |

## NORMAL VALUES FOR SEMEN

| | |
|---|---|
| Volume | 2-5 ml., usually 3-4 ml. |
| Liquefaction | Complete in 15 minutes |
| pH | 7.2-8.0, average 7.8 |
| Leukocytes | Occasional or absent |
| Count | 60-150 million/ml. |
| | Below 60 million/ml. is abnormal |
| Motility | 80% or more motile |
| Morphology | 80-90% normal forms |

## NORMAL VALUES FOR SEROUS FLUIDS
(pleural, pericardial, peritoneal)

| | |
|---|---|
| pH | 6.80-7.60 |
| Specific gravity | 1.010-1.026 |

Protein

| | |
|---|---|
| Total | 0.30-4.10 Gm./100 ml. |
| Albumin | 50.5-69.8% |
| Globulin | 29.5-45.8% |
| Fibrinogen | 0.3-4.5% |

# FUNCTIONAL TESTS

## RENAL FUNCTION TESTS

Clearance tests (corrected to 1.73 sq. meters body surface area)

| | | |
|---|---|---|
| Glomerular filtration rate (G.F.R.) | | |
| Inulin clearance | Males | 110-150 ml./min. |
| Mannitol clearance | Females | 105-132 ml./min. |
| Endogenous creatine clearance | | |
| Renal plasma flow (R.P.F.) | | |
| p-Aminohippurate (P.A.H.) | Males | 560-830 ml./min. |
| Diodrast | Females | 490-700 ml./min. |
| Filtration fraction (F.F.) | | |
| $F.F. = \frac{G.F.R.}{R.P.F.}$ | Males | 17-21% |
| | Females | 17-23% |
| | Standard | 40-65 ml./min. |
| Urea clearance (Cu) | Maximal | 60-100 ml./min. |
| Concentration and dilution | Specific gravity > 1.025 on dry day<br>Specific gravity < 1.003 on water day | |
| Maximal Diodrast excretory capacity $T_{M_D}$ | Males | 43-59 mg./min. |
| | Females | 33-51 mg./min. |
| Maximal glucose reabsorptive capacity $T_{M_G}$ | Males | 300-540 mg./min. |
| | Females | 250-350 mg./min. |
| Maximal P.A.H. excretory capacity $T_{MPAH}$ | 80-90 mg./min. | |
| Phenosulfonphthalein excretion (P.S.P.) | 25% or more in 15 min.<br>40% or more in 30 min.<br>55% or more in 2 hours<br>After injection of 1 ml. P.S.P. intravenously | |

## LIVER FUNCTION TESTS

| | |
|---|---|
| Bromsulfalein (B.S.P.) | Less than 5% remaining in serum 45 minutes after injection of 5 mg./kg. of body weight. |
| Cephalin cholesterol flocculation | 0-2 + in 48 hours. |
| Cholinesterase (pseudocholinesterase), serum | 0.5 pH units or over/hour. |
| Galactose tolerance | Excretion of not more than 3.0 gm. galactose in the urine 5 hours after ingestion of 40 gm. of galactose. |
| Glycogen storage | Increase of blood glucose 45 mg./100 ml. over fasting level 45 minutes after subcutaneous injection of 0.01 mg./kg. body weight of epinephrin. |

## FUNCTIONAL TESTS—*(Cont'd)*

| | |
|---|---|
| Hippuric acid | Excretion of 3.0-3.5 gm. hippuric acid in urine in 4 hr. after ingestion of 6.0 gm. sodium benzoate, *or* Excretion of 0.7 gm. hippuric acid in urine in 1 hr. after intravenous injection of 1.77 gm. sodium benzoate. |
| Thymol turbidity | 0-5 units. |
| Zinc turbidity | 2-12 units. |

## PANCREATIC (ISLET) FUNCTION TESTS

| | |
|---|---|
| Glucose tolerance tests | Patient should be on diet containing 300 gm. of carbohydrate per day for 3 days prior to test. Values given are for true glucose; with Folin method values are approximately 20 mg./100 ml. higher. |
| Oral | After ingestion of 100 gm. of glucose or 1.75 gm. glucose per kg. body weight, blood glucose not more than 160 mg./100 ml. after 60 minutes, 140 mg./100 ml. after 90 minutes and 120 mg./100 ml. after 120 minutes. |
| Intravenous | Blood glucose does not exceed 200 mg./100 ml. after infusion of 0.5 gm. of glucose per kg. body weight over 30 minutes. Glucose concentration falls below initial level at 2 hours and returns to preinfusion levels in 3 or 4 hours. |
| Cortisone-glucose tolerance test | The patient should be on diet containing 300 gm. of carbohydrate per day for 3 days prior to test. At 8½ and again 2 hours prior to glucose load, patient is given cortisone acetate by mouth (50 mg. if patient's ideal weight is less than 160 lbs., 62.5 mg. if ideal weight is greater than 160 lbs.). An oral dose of glucose, 1.75 gm. per kg. ideal body weight, is given and blood samples are taken at 0, 30, 60, 90 and 120 min. Test is considered positive if true blood glucose exceeds 160 mg./100 ml. at 60 min., 140 mg./100 ml. at 90 min., and 120 mg./100 ml. at 120 min. |

## PULMONARY FUNCTION TESTS

*See following table*

*Measurements of Principal Lung Volumes and Formulas for Their Prediction in Normal Subjects*

| | AGE 16-34 | | AGE 35-49 | | AGE 50-69 | |
|---|---|---|---|---|---|---|
| | Women | Men | Women | Men | Women | Men |
| Vital capacity, supine (ml.) | 2312-4150 | 2792-4950 | 2212-3435 | 3300-5240 | 1570-3525 | 2184-5429 |
| Maximum breathing capacity, standing (L./min.) | 63.6-117.5 | 82-169 | 47-114 | 86-144.5 | 49-101.5 | 58-139 |
| Ventilation, resting (L./min./sq. M. body surface) | 2.55-4.27 | 3.1-4.5 | 2.4-3.71 | 2.6-4.0 | 2.53-3.95 | 3.2-4.9 |
| Oxygen consumption, resting (ml./min./sq. M. body surface) | 111-149 | 129-186 | 109-136 | 118-156 | 105-150 | 107-165 |
| Predicted (calculated) total capacity (supine) | $\frac{\text{Vital capacity}}{80} \times 100$ | | $\frac{\text{Vital capacity}}{76.6} \times 100$ | | $\frac{\text{Vital capacity}}{69.2} \times 100$ | |
| Ratio $\frac{\text{Residual volume}}{\text{Total capacity}} \times 100$ (supine) | 20 | | 23.4 | | 30.8 | |
| Predicted (calculated) vital capacity, supine (ml.) | Women : [ 21.78-(0.101 x age in yrs.) ] x height in cm.<br>Men: [ 27.63-(0.112 x age in yrs.) ] x height in cm. | | | | | |
| Predicted (calculated maximum breathing capacity standing (L./min.) | Women : [ 71.3-(0.474 x age in yrs.) ] x sq. M. body surface<br>Men: [ 86.5-(0.522 x age in yrs.) ] x sq. M. body surface | | | | | |

## CARDIAC FUNCTION TESTS

| | | |
|---|---|---|
| Blood volume | | 8.5-9.0% of body weight. |
| Cardiac output | | 3.0 liters/min. /sq. meter body surface area. |
| Cardiac pressures | Right atrium | Mean, 0-5 mm. Hg. |
| | Right ventricle | Systolic 20-30 mm. Hg.<br>Diastolic 0-5 mm. Hg. |
| | Pulmonary artery | Systolic 20-30 mm. Hg.<br>Diastolic 7-12 mm. Hg.<br>Mean 12-17 mm. Hg. |
| Circulation time | Arm to tongue | 10-16 seconds |
| Venous pressure | | 60-120 mm. water. |

## GASTROINTESTINAL ABSORPTION TESTS

| | |
|---|---|
| d-Xylose absorption test | After an 8-hour fast 10 ml./kg. body weight of a 5% solution of d-xylose |

| | |
|---|---|
| | is given by mouth. Nothing further by mouth is given until the test has been completed. All urine voided during the following 5 hours is pooled, and blood samples are taken at 0,60 and 120 min. Normally 26% (range 16-33%) of ingested xylose is excreted within 5 hours, and the serum xylose reaches a level between 25 and 40 mg./100 ml. after 1 hour and is maintained at this level for another 60 minutes. |
| Vitamin A absorption test | A fasting blood specimen is obtained and 200,000 units of vitamin A in oil is given by mouth. Serum vitamin A level should rise to twice fasting level in 3 to 5 hours. |

## METABOLIC FUNCTION TESTS

| | |
|---|---|
| Basal metabolic rate | −10% to +10% of mean standard |
| Creatine tolerance | 70% ingested creatine retained in adults |
| Glucose tolerance, 100 Gm. glucose or 1.75 Gm. glucose/Kg. body weight, p.o. | Blood sugar not more than 180 mg./100 ml. after ½ hr., return to normal in 2 hr., sugar not present in any urine specimen |
| Radioactive iodine ($I^{131}$) | |
| Uptake | 20-50% of administered dose |
| Excretion | 30-70% of administered dose in 24 hr. following tracer dose, provided renal function is normal |
| Protein-bound, Serum or plasma | < 0.3% of administered dose per liter of plasma at 72 hr. following tracer dose |
| Conversion ratio | < 35% at 24 hr. |
| Water test (Soffer) | 80% excretion of a 1,500 ml. water load in 4 hr. |

## ADRENAL-PITUITARY FUNCTION TESTS

| | |
|---|---|
| Insulin tolerance test | Blood glucose usually falls to 50% of fasting level in 20 to 30 minutes with return to normal levels in 90 to 120 minutes after intravenous administration of 0.1 unit crystalline insulin per kg. body weight. |

## FUNCTIONAL TESTS—*(Cont'd)*

| | |
|---|---|
| Adrenocortical inhibition test<br>△-1, 9, -∝-fluorocortisone or<br>16-methyl-∝-hydrocortisone | 0.5 mg. p.o. every 6 hours of either drug reduces excretion of 17-hydroxycorticoids from 4-15 mg./24 hrs. to a level of less than 2 mg./24 hrs. |
| Corticotropin (ACTH) response tests | |
| Eosinophil count (Thorn test) | Four hours after 25 U.S.P. units of ACTH I.M. decrease in eosinophil count should exceed 50% of the initial level. |
| Plasma 17-hydroxycorticoids | After 8-hour infusion of 25 U.S.P. units of ACTH, plasma 17-hydroxycorticoids rise from a normal level of 5-25 microgm./100 ml. to 35-55 microgm./100 ml. |
| Urinary steroids | After 8-hour infusion of 25 U.S.P. units of ACTH, urinary 17-hydroxycorticoids increase 200 to 400% and urinary 17-ketosteroids increase 50 to 100%. |

## THYROID FUNCTION TESTS

| | |
|---|---|
| Radioactive iodine ($I^{131}$) uptake | 20-50% of administered dose in 24 hrs. |
| Radioactive iodine ($I^{131}$) excretion | 30-70% of administered dose in 24 hrs. |
| Radioactive iodine, protein bound | Less than 0.3% of administered dose per liter of plasma at 72 hours. |

# OBSTETRIC TABLE

The calculation is made from the first day of the last menstrual period

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **JANUARY** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | **31** | **JANUARY** |
| OCTOBER | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | NOVEMBER |
| **FEBRUARY** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | | | | **FEBRUARY** |
| NOVEMBER | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 1 | 2 | 3 | 4 | 5 | | | | DECEMBER |
| **MARCH** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | **31** | **MARCH** |
| DECEMBER | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 1 | 2 | 3 | 4 | 5 | JANUARY |
| **APRIL** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | | **APRIL** |
| JANUARY | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 1 | 2 | 3 | 4 | | FEBRUARY |
| **MAY** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | **31** | **MAY** |
| FEBRUARY | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | MARCH |
| **JUNE** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | | **JUNE** |
| MARCH | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 1 | 2 | 3 | 4 | 5 | 6 | | APRIL |
| **JULY** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | **31** | **JULY** |
| APRIL | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | MAY |
| **AUGUST** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | **31** | **AUGUST** |
| MAY | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | JUNE |
| **SEPTEMBER** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | | **SEPTEMBER** |
| JUNE | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | | JULY |
| **OCTOBER** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | **31** | **OCTOBER** |
| JULY | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | AUGUST |
| **NOVEMBER** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | | **NOVEMBER** |
| AUGUST | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 1 | 2 | 3 | 4 | 5 | 6 | | SEPTEMBER |
| **DECEMBER** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** | **16** | **17** | **18** | **19** | **20** | **21** | **22** | **23** | **24** | **25** | **26** | **27** | **28** | **29** | **30** | **31** | **DECEMBER** |
| SEPTEMBER | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | OCTOBER |

Paralty Receipt No: 47870

# THE PRICELESS INGREDIENT

In the City of Bagdad lived Hake
the Wise One, and many people went to him for counsel which he gave freely
all, asking nothing in return.

There came to him a young man who had spent much but got little, and sa
"Tell me, Wise One, what shall I do to receive the most for that which I spend
Hakeem answered, "A thing that is bought or sold has no value unless it conta
that which cannot be bought or sold. Look for the Priceless Ingredient." "But, wh
is this Priceless Ingredient?" asked the young man.

Spoke then the Wise One: "My son, the Priceless Ingredient of every product
the market-place is the Honor and Integrity of him who makes it. Consider h
name before you buy."

SQUIBB QUALITY—THE PRICELESS INGREDIENT